

his .

Med
A.

AMERICAN JOURNAL
OF
DISEASES OF CHILDREN

EDITORIAL BOARD

H. F. HELMHOLZ, Evanston, Ill.

L. EMMETT HOLT, New York City

DAVID M. COWIE, Ann Arbor, Mich

FRITZ B. TALBOT, Boston

EDWIN E. GRAHAM, Philadelphia

JOHN HOWLAND, Baltimore

VOLUME 19
1920

210795-
29:3:27

PUBLISHERS
AMERICAN MEDICAL ASSOCIATION
CHICAGO, ILL.

RJ

1

A5

v. 19

cop. 2

CONTENTS OF VOLUME 19

JANUARY, 1920. NUMBER 1

	PAGE
A STUDY OF ACHONDROPLASIA. INTRODUCING A NEW SYMPTOM—WEDGE-SHAPED VERTEBRA. THOMAS FOSTER WHEELDON, A.M., M.D., RICHMOND, VA.	1
THE FOOD VALUE OF THE MILK OF THE WATER BUFFALO. WILLIAM W. CADBURY, M.D., CANTON, CHINA.....	38
DEXTROSE TOLERANCE IN ATROPHIC INFANTS. P. M. MATTILL, K. M. MAYER AND L. W. SAUER, CHICAGO.....	42
A CASE OF HYPERSENSITIVENESS TO COW'S MILK. EDWARDS A. PARK, M.D., BALTIMORE	46
CLINICAL DEPARTMENT: A CASE OF ANOMALY OF THE DIAPHRAGM WITH HERNIATION INTO THE THORAX OF CERTAIN VISCERA RESULTING IN A GASTRIC AND INTESTINAL OBSTRUCTION. L. R. DEBUYS, B.S., M.D., NEW ORLEANS	55
PROGRESS IN PEDIATRICS: RÉSUMÉ ON THE CIRCULATORY SYSTEM. REVIEW OF LITERATURE OF 1917, 1918 AND 1919. HENRIETTA CALHOUN, M.B., IOWA CITY	62

FEBRUARY, 1920. NUMBER 2

THE ETIOLOGY OF ARTHRITIS DEFORMANS IN CHILDREN. ALBERT H. BYFIELD, M.D., IOWA CITY.....	87
CALCIUM METABOLISM OF INFANTS AND YOUNG CHILDREN, AND THE RELATION OF CALCIUM TO FAT EXCRETION IN THE STOOLS. L. EMMETT HOLT, M.D., ANGELIA M. COURTNEY AND HELEN L. FALES, NEW YORK.....	97
INCIDENCE OF PROTEIN SENSITIZATION IN THE NORMAL CHILD. HORACE MITCHELL BAKER, M.D., BOSTON.....	114
FOREIGN BODIES IN THE AIR AND FOOD PASSAGES. EDWIN E. GRAHAM, M.D., PHILADELPHIA	119
AURICULOVENTRICULAR HEART BLOCK IN CHILDREN, WITH REPORT OF A CASE. J. A. E. EYSTER AND W. S. MIDDLETON, MADISON, WIS.....	131
ABSCESS OF THE LUNGS IN INFANTS AND CHILDREN. HARRY WESSLER, M.D., AND HERMAN SCHWARZ, M.D., NEW YORK.....	137
THE ELIMINATION OF ACETONE BODIES DURING INFECTIOUS FEVER. BORDEN S. VEEDER, M.D., ST. LOUIS, AND MEREDITH R. JOHNSTON, M.D., CAPTAIN, M. C., U. S. ARMY.....	141
CLINICAL DEPARTMENT: A REPORT OF TWO CASES OF CONGENITAL STRICTURE OF THE ESOPHAGUS. JOHN LOVETT MORSE, A.M., M.D., BOSTON.....	144
PROGRESS IN PEDIATRICS: RECENT WORK IN ANATOMY, PHYSIOLOGY AND PATHOLOGY OF INFANCY AND CHILDHOOD. JAMES B. HOLMES, M.D., BALTIMORE	148

MARCH, 1920. NUMBER 3

DILATATION OF THE COLON IN CHILDREN. ALFRED EDWARD MEYERS, M.D., SAN FRANCISCO	167
OSTEOGENESIS IMPERFECTA CONGENITA. H. M. McCLANAHAN, M.D., AND W. W. WILLARD, PH.G., OMAHA.....	181
CHONDRODYSPLASIA; MULTIPLE CARTILAGINOUS EXOSTOSES. REPORT OF CASES. HUGH L. DWYER, M.D., KANSAS CITY, MO.....	189
CALCIUM METABOLISM OF INFANTS AND YOUNG CHILDREN, AND THE RELATION OF CALCIUM TO FAT EXCRETION IN THE STOOLS. PART 2.—CHILDREN TAKING A MIXED DIET. L. EMMETT HOLT, M.D., ANGELIA M. COURTNEY AND HELEN L. FALES, NEW YORK.....	201
A NOTE ON RENAL FUNCTION IN SCARLET FEVER. BORDEN S. VEEDER, ST. LOUIS, AND MEREDITH R. JOHNSTON, CAPTAIN, M. C., U. S. ARMY.....	223
AN IMPROVED NEEDLE FOR SINUS THERAPY. ALTON GOLDBLOOM, M.D., NEW YORK	229
PROGRESS IN PEDIATRICS: REVIEW OF LITERATURE ON RESPIRATORY DISEASES. LOUIS C. SCHROEDER, M.D., NEW YORK.....	231

CONTENTS OF VOLUME 19

APRIL, 1920. NUMBER 4

	PAGE
INFANT AND CHILD MORTALITY, INCLUDING MISCARRIAGES AND STILL-BIRTHS. HERMAN SCHWARZ, M.D., NEW YORK.....	249
RESULTS OF SOME EXPERIMENTAL WORK WITH SODIUM CACODYLATE ON ATHREPTIC INFANTS. FLOYD S. CLARKE, M.D., AND ANDREW DOW, M.D., OMAHA	260
PROGNOSIS IN OPERATED CASES OF HYPERTROPHIC STENOSIS OF PYLORUS. ALTON GOLDBLOOM, M.D., AND RALPH C. SPENCE, M.D., NEW YORK....	263
STUDIES WITH A NEW METHOD FOR DETERMINING THE COAGULATION TIME OF THE BLOOD IN THE NEW-BORN. F. C. RODDA, M.D., MINNEAPOLIS....	269
CLINICAL DEPARTMENT: ROENTGEN-RAY DEMONSTRATION OF ABNORMALITIES OF THE GASTRO-INTESTINAL TRACT IN CHILDREN. CHARLES GILMORE KERLEY, M.D., NEW YORK.....	277
PROGRESS IN PEDIATRICS: RÉSUMÉ OF LITERATURE ON TUBERCULOSIS IN CHILDREN DURING 1918 AND 1919. MAY MICHAEL, M.D., CHICAGO....	287

MAY, 1920. NUMBER 5

SCORBUTIC BEADING OF THE RIBS. ALFRED F. HESS, M.D., AND LESTER J. UNGER, M.D., NEW YORK.....	331
WATER RETENTION IN PNEUMONIA. HERBERT O. LUSSKY, M.D., AND HUGO FRIEDSTEIN, M.D., CHICAGO.....	337
PRENATAL SYPHILIS, WITH A PLEA FOR ITS STUDY AND PREVENTION. JOHN A. KOLMER, M.D., PHILADELPHIA.....	344
THE ANTINEUROTIC AND GROWTH STIMULATING PROPERTIES OF ORANGE JUICE. ALBERT H. BYFIELD, M.D., AND AMY L. DANIELS, PH.D., WITH THE COOPERATION OF ROSEMARY LOUGHLIN, M.S., IOWA CITY.....	349
FLUID INJECTIONS IN DEHYDRATED INFANTS. STAFFORD MCLEAN AND CHARLES A. LANG, M.D., NEW YORK.....	359
THE LENGTH OF THE LARGE AND SMALL INTESTINE IN YOUNG CHILDREN. LEWIS ROBBIN, M.D., NEW YORK.....	370
TREATMENT OF BIRTH FRACTURES AT FORDHAM HOSPITAL. SAMUEL W. BOORSTEIN, M.D., NEW YORK.....	375
CRANIOTABES AND BEADING OF THE RIBS AS SIGNS OF RACHITIS. HERMAN SCHWARTZ, M.D., NEW YORK.....	384
ARTIFICIAL INFANT FEEDING: GIVE THE BABY ENOUGH. MAURICE OSTHEIMER, M.D., PHILADELPHIA	386
CLINICAL DEPARTMENT: SUBCUTANEOUS EMPHYSEMA IN AN INFANT THREE DAYS OLD. HAROLD K. FABER, M.D., SAN FRANCISCO.....	388
PROGRESS IN PEDIATRICS: REVIEW OF THE LITERATURE OF THE PAST FIVE YEARS ON ANAPHYLAXIS AND RELATED PHENOMENA. A. R. CUNNINGHAM, M.D., BOSTON.....	392

JUNE, 1920. NUMBER 6

THE EFFECT OF INTRAVENOUS INJECTIONS OF CALCIUM IN TETANY AND THE INFLUENCE OF COD LIVER OIL AND PHOSPHORUS IN THE RETENTION OF CALCIUM IN THE BLOOD. ALAN BROWN, M.B.; IDA F. MACLACHLAN, B.A., AND ROY SIMPSON, M.B., TORONTO.....	413
THE NITROGENOUS AND SUGAR CONTENT OF THE BLOOD OF THE NEW-BORN. J. P. SEDGWICK, B.S., M.D., AND MILDRED R. ZIEGLER, M.S., MINNEAPOLIS	429
ALLERGY IN INFANTS AND CHILDREN. OSCAR M. SCHLOSS, M.D., NEW YORK.	433
FORDYCE'S DISEASE AS PSEUDO-KOPLIK SPOTS AND A CAUSE OF MISTAKES IN THE DIAGNOSIS OF MEASLES. JOSEPH C. REGAN, M.D., BROOKLYN..	455
THE BACILLUS OF PFEIFFER IN INFLAMMATIONS OF THE RESPIRATORY TRACT IN CHILDREN. MARTHA WOLLSTEIN, M.D., AND RALPH C. SPENCE, NEW YORK	459
BULLOUS ERUPTION COMPLICATING MEASLES. FRANK C. NEFF, M.D., KANSAS CITY, MO.....	469
CLINICAL DEPARTMENT: HEMORRHAGE INTO THE SPINAL CORD AT BIRTH. CHARLES W. BURR, M.D., PHILADELPHIA.....	473
PROGRESS IN PEDIATRICS: VON PIRQUET'S FEEDING SYSTEM. HAROLD K. FABER, M.D., SAN FRANCISCO.....	478

American Journal of Diseases of Children

Vol. 19

JANUARY, 1920

No. 1

A STUDY OF ACHONDROPLASIA *

INTRODUCING A NEW SYMPTOM — A WEDGE-SHAPED VERTEBRA

THOMAS FOSTER WHEELDON, A.M., M.D.

RICHMOND, VA.

INTRODUCTION

Ita P. appeared in the orthopedic outpatient department of the Children's Hospital for treatment because of a "bunch" on her back. As usual, a roentgen-ray examination was made. The plates showed widely separated vertebral bodies with a peculiar wedge-shaped vertebra at the point of the "bunch." As this did not seem to be due to any of the more common processes, further study was instituted.

Following this, Jansen's "Achondroplasia" was studied, and it was while studying this that the idea suggested itself that the peculiar wedge-shaped vertebra might easily be a result of his "amnio pressure," although he makes no mention of this condition. Furthermore, the significance of the following statement of G. Elliot Smith (of the University of Manchester) became evident. "His (Jansen's) hypothesis cannot fail to serve the even greater purpose of stimulating research, by giving a new point of view, an illuminating suggestion, which is certain to become the nucleus of a whole series of investigations."

The whole work has been done under the helpful supervision of Dr. Robert W. Lovett, who first suggested that the wedge-shaped vertebra be studied further, and who added that Jansen's conclusions might shed some light on the subject. To him is due full credit for stimulating the present inquiries.

The roentgen-ray examinations were made by Miss Dorothy Weil of the roentgen department of the Children's Hospital. Mr. J. V. Footman developed and reduced the plates.

* Because of lack of space, a large number of figures have been omitted. In the original article, there are complete series of photographs of front, side and back views of each of the children with photographs of most of the hands and feet individually. Also there is a roentgenogram of every bone of each child.

For comparison, two complete photographic and roentgenologic series of normal children are shown.

In measuring the cases the method of Dr. Joseph I. Grover of Boston was used.

I take this opportunity to thank the trustees, who through Miss I. C. Smith, superintendent, placed at our disposal the facilities of the Children's Hospital, where all the cases were studied.

REVIEW OF LITERATURE

G. Elliot Smith (1912) has the following to say of dwarfs:

"Nearly fifty centuries ago the most treasured gift the general in command of an Egyptian Expedition brought for his Pharaoh from a foreign country was a dwarf to entertain him and his court by his antics (Schiaparelli: *Una Tomba Egiziana inedita della Via Dinastia*, Rome, 1893), and from that time onward throughout the ages, even until the present day, the quaintness and not overdélicate wit of the dwarf have ever secured him a place in the court of the ruler of Egypt.

"Moreover, the ancient Egyptians selected the dwarf with his misshapen head and limbs as the prototype of Bes, their god of sexual intercourse (Quibell: *Excavations at Saqqara, 1905-1906*, Cairo Museum Reports) and they represent him with genitalia of phenomenal proportions—a fact which assumes special significance in the light of the discussion to be found in this (Jansen, 1912) monograph.

"From this it is evident that the distinctive structural peculiarities and functional proclivities of the dwarf have been realized from the very dawn of history; and no doubt even long before man learned to record his thoughts in written characters he had become familiar with the achondroplastic. But the problem of explaining the genesis and significance of the curious series of physical and mental traits peculiar to the dwarf has always baffled the investigator, even though many of the greatest clinicians, pathologists and embryologists of the last century have attempted to resolve its difficulties.

"The recent appreciation of the marvelous influences exerted in ways so manifold by the internal secretions of a whole series of organs has not unnaturally riveted attention mainly on such factors as the influence of the pituitary body, the thyroid and the sexual organs for an explanation of nanism. But so far the pursuit has been in vain."

Murk Jansen (1912) adds: "From the earliest times recorded in history we meet with scattered instances of dwarfs; thus the ancient Egyptians worshipped the god "Ptah" (Porak et Durante, 1905), who shows (that) stunting of the extremities characteristic of achondroplasia. In the Middle Ages we find achondroplasts at court as 'fools.' The grotesque proportions of these otherwise healthy and ever robust individuals, as well as their liveliness and perhaps a suspicion of impu-

dence, which often characterizes them, may have rendered them particularly fitted for this position.

"In recent times the lot of dwarfs, no longer found in palaces and temples, has been cast amid less exalted surroundings; but, on account of their sense of the burlesque, they afford a lively source of amusement in various places of public entertainment.



Fig. 1.—Emily S. Total length 70.4 cm. This picture shows (a) the brachycephalic head; (b) the broad face; (c) the flattened and sunken nasal bridge; (d) the cretinistic facies; (e) the rather short neck; (f) the short extremities; (g) the large amount of subcutaneous fat.

"During the last forty years this remarkable form of dwarf growth has so far attracted the attention of scientists as to secure their careful study in tracing its causes. An extensive literature on the subject has arisen, in which the dwarf is described by almost twenty different

names, most of them borrowed from the Greek. From this it is evident that each investigator formed his own idea of its nature, but failed to procure convincing proofs."

Parrot (1878) first used the terms "achondroplasia" in describing the affection which he recognized as an independent form of disease in a number of fetuses. This term was adopted by Porak (1891) and P. Marie (1900) in their papers. Osler (1897) says, "On August 4, 1886, when at Cacouna in the Province of Quebec, I was asked to see two cretins, and found them remarkable rhacitic dwarfs belonging to this type," and "it was some years later that I learned the true nature of the affection, namely, the chondrodystrophia foetalis." Osler also,



Fig. 2.—Emily S. This picture shows the "main en trident" and prominent epiphyses.

with others, for years used the term "fetal rickets." Kaufmann (1892), in the meantime, described the pathologic condition in achondroplasia and adopted the name "chondrodystrophia." "It is," he says, "a disturbance of the endochondral ossification while the ossification on the side of the periosteum is perfectly normal." He distinguished three forms: (1) chondrodystrophia hypoplastica, in which the principle element is a simple cessation in the growth of the cartilage; (2) chondrodystrophia malacica, in which the arrest of the growth is dependent on the softening of the cartilage; (3) chondrodystrophia hyperplastica, in which we are concerned not simply with an arrest of the growth of the cartilage, but with an excessive growth abnormal in its direction (Bullard and George, 1908). Jansen (1912) prefers

the name achondroplasia for he says, "Kaufmann in Germany afterwards adopted the name "chondrodystrophia," thereby indicating that the affection is distinguished less by an absence of the 'cartilage' than by a disturbance of its nutrition. In what follows we shall, however, see that, on the one hand, the trophic disturbance may leave some cartilaginous formations unaffected, while, on the other hand, it may extend even to bones formed in membrane. We shall, therefore, for



Fig. 3.—Emily S. Roentgenogram showing: (a) the brachycephalic head; (b) the small sella turcica; (c) the narrowed nasopharynx.

the present, keep to the name sanctioned by use — achondroplasia, by which we understand an affection characterized by a congenital shortness of the extremities and the base of the skull." Although at present the terms "achondroplasia," "fetal rickets," and "chondrodystrophia" are used interchangeably (Bradford and Lovett, 1915; Whitman, 1917), most writers' descriptions of the disease agree more fully with that of Jansen, and it seems only consistent to use the name he so well vindicates.

Morse (1902) in reviewing the American cases, says, "Very few cases of this condition have been reported in this country and the diagnosis of several of these is open to considerable doubt." For the sake of completeness, I have included his cases in my bibliography, and in addition all other American and foreign cases I could find.

REVIEW OF JANSEN'S "ACHONDROPLASIA"

Jansen (1912) has so skillfully arranged the mass of facts concerning achondroplasia that it seems most profitable to consider our own cases in the light of his work. For that reason, the first main division of his memoir, "The Nature of Achondroplasia," will be reviewed now. The second main division, "The Cause of Achondroplasia," will be reviewed later.

Jansen divided the nature of achondroplasia into two groups of symptoms: (1) Those of dwarf growth, and (2) those which are the result of infolding. "The former," he says, "are quite obvious and lend themselves to the recognition of the achondroplast even at a distance. The latter, on the contrary, are less conspicuous, and have thus, for the greater part, passed unnoticed hitherto. It is these very mechanical malformations, however, which will prove useful in tracing the cause of achondroplasia."

The symptoms of dwarf growth include those involving the extremities, pelvis, vertebral column, thorax and other parts. The extremities are too short, while the trunk is equal in development to that of a normal child of the same age.

He says, "Notice that the shortness of the extremities is not due to any crookedness or bending of the bones, as in rickets or osteomalacia, nor the result of multiple fractures, as in osteogenesis imperfecta; nor is it due to absence of the proximal parts, as in phocomelia or congenital deficiency of the femur, and so forth; nor of the distal parts, as in congenital amputations and in hemimelia. All the bones are present, scarcely or not at all bent; they are simply too short. This shortness affects the proximal more than the distal parts of the extremities, and is called "micromelie rhizomelique," although, as appears in the comparatively broad hand and short fingers, the peripheral parts are not unaffected."

"The "main en trident" is present, the second and fifth metacarpals diverging more than the normal 32 degrees, and usually as much as 40 degrees. The fingers do not group themselves about the middle finger. In addition, the bones of the achondroplastic hand are not only too short, but also too slender, the latter in a less degree than the former. The pelvis lags behind in development, when compared with the other parts of the trunk. The pelvis is small in pro-



Fig. 4.—Emily S. Roentgenogram showing what Jansen says is a tendency of the organs of achondroplasts to be "gaseous."

portion to the size of the body, its cavity is funnel shaped, and the alae ossium ilii are relatively poorly developed.

The vertebral column is often affected. Its length may not be more than one half that of the normal. Occasionally, the size of the vertebral bodies diminishes from neck to sacrum.

The skull, even in the most serious form of achondroplasia known, escapes the dwarf growth. It may be deformed, having a backward basis cranii, more (unossified) cartilage in the petrosal parts of the temporal bones and the basilar, and a short hard palate, but it does not become dwarfed.

The chest is often shortened and consequently is too small for the proper accommodation of the vital organs. The caudal circumference is pressed upward, so that the sternum is directed almost horizontally and its shape comes to resemble a calotte.

The skin is often loose and arranged in oblique and transverse folds reminding one of a pair of knickerbockers.

Achondroplasia occurs in various degrees; in the most serious forms the growth of the oldest parts of the skeleton (the whole of the vertebral column) is defective. They are not viable. Only the slighter forms may survive; in them the trunk reaches the normal length, or very nearly; it is chiefly the extremities — with the pelvis — that are affected.

Henri Dufour (1906) recently described "atypical forms of achondroplasia." These include forms in which the extremities are only very slightly shortened, and forms in which the fourth metacarpal or metatarsal bone is relatively short in otherwise perfectly normal individuals (Chevallier (1910). Jansen would prefer substituting "slightest" for "atypical" and apply it to the former. The latter forms he would group in the manifold forms of *kakomelia*.

In addition to the characteristic phenomena of growth disturbance in achondroplasia there are often present a group of symptoms connected with sex. A two-year-old girl may have well developed pubic hair. The sexual appetite may be enhanced.

Let us now turn to the symptoms of infolding. These appear to be the direct result of mechanical forces modifying the form of the fetus.

While, as we have seen, except in the more severe forms, the dwarfing process spares the skull, it is the skull that is most affected by the mechanical malformations. The basis cranii is shortened while the breadth of the skull exceeds the normal — brachycephaly (Parhon, Shunda and Zalplachta, 1905). The height of the skull is often increased and the circumference enlarged. Jansen (1912) says that the intellect is often normal and may be above the average; but

Parhon, Shunda and Zalplachta observed that it usually stands in inverse proportion to the circumference. Kaufmann (1892) very clearly pictures the malformation found in the skull. In all of his figures the shortening of the basis cranii and in some of them the premature fusion of its parts, are to be seen. It seems, however, that both he and Virchow overlooked the causes of these conditions. In explaining these facts Jansen (1912) advances the supposition that during its fetal development the achondroplastic skull is submitted to a pressure in front, against the face, and behind, against the occiput. The consequence of this pressure is:

1. That the nasal bone and the squama occipitalis approach each other; that the skull and its base are shortened, thus causing the ossification centers of the basilar bone to come too close together in an early stage.



Fig. 5.—Ita P. Aged 1½ years. Total length 78.3 cm. This picture shows the dorsolumbar kyphos which does not disappear even on lying down.

2. A lessening of the sagittal dimensions of the mouth cavity with a displacement of the hard palate toward the basis cranii (a narrowing of the choanae).

3. Either a kyphosis baseos cranii or a sagittal narrowing of the foramen magnum.

As a result there may be either a depression of the nasal bridge only or a flattening of the nose in toto. The narrowing of the choanae may cause a noisy, snoring respiration and may be mistaken for adenoid vegetations.

With the change in the shape of the skull the brain conforms so that when laid by the side of a normal brain of the same age the characteristic deformity is easily seen.

In addition the sella tureica may be reduced in size even to total obliteration, and, regarding the pituitary body which lies in it, Jansen draws the conclusion from a review of the literature that it is reduced

in size in the serious cases of achondroplasia, and little or not at all in the slightest forms.

Turning now to the spine, we recognize the malformation by which the achondroplast is distinguished from the normal. The three sagittal curvatures which occur in the normal spine of new-born infants are not present. The spine may be curved backward, the normal lumbar



Fig. 6.—Ita P. Roentgenogram showing: (a) the brachycephalic head; (b) the narrowed nasopharynx; (c) the kyphosis basis cranii; (d) the queer angle of the sella turcica; (e) the tendency for the alveoli to project backward.

lordosis being replaced by a dorsolumbar arcuate kyphosis. This is often first noticed in infants because they lie "bent-up" and may persist to adult life where it seems to be a more constant symptom of achondroplasia even than the depression in the nosebridge which is not infrequently missing.

REPORT OF CASES

CASE 1.—Emily S.; Age, 1 $\frac{1}{2}$ years; Italian parentage.

Family History.—Negative for tuberculosis, rheumatism, joint diseases, central nervous system disturbances and venereal diseases. No other deformity in the family.

Patient's History.—Negative. Denies any previous illness.

Present Illness.—Mother brings the child into the hospital because of a "bump on her back." Duration of life. Child recommended to house for study.

Physical Examination.—General; poorly developed but well nourished child.

Head: Brachycephalic, prominent frontal bosses, open anterior fontanel, broad face, flattened and sunken nasal bridge, cretinistic facies.

Neck: Rather short.

Upper Extremities: Very short for length of trunk, epiphyses easily felt.

Chest: Harrison's groove and rosary present, the sternum projects forward at an increased angle, the nipples are noted to be very high.

Abdomen: "Pot-belly," liver and spleen palpable.

Spine: Definite low dorsal rounded kyphos on sitting and lying.

Lower Extremities: Very short for length of trunk, epiphyses are easily felt, legs held in abduction when lying on back, an enormous amount of fat hangs from the legs like pantaloons.

Neuromuscular: Child cannot walk or stand so far as is known, child sits in leaning forward posture usually, supporting the body by the hands resting on the knees.

Measurements.—See table.

Laboratory Examination.—Tests for tuberculosis and syphilis were negative.

Mental Examination.—Intelligence normal for age.

CASE 2.—Ita P.; 1 $\frac{1}{2}$ years; Italian parentage.

Family History.—Negative for tuberculosis, rheumatism, joint diseases, central nervous system disturbances and venereal disease. Four other children living and well. No other deformities in the family.

Patient's History.—Negative. Denies any previous illness. Normal birth history.

Present Illness.—Mother brings the child to the hospital because of a "bunch on its back" present since the age of 2 months. The "bunch" has been growing larger. Child recommended to house for study.

Physical Examination.—General: fairly well developed and nourished baby.

Head: Brachycephalic, marked prominence of the parietal and temporal bosses, broad face suggestive of cretinism, broad nasal bridge, ears project noticeably from the sides of the head.

Neck: Slightly shortened.

Upper Extremities: Short for length of trunk, marked epiphyseal enlargement, enormous amount of fat hanging from arms, fingers seem thickened.

Chest: Marked rosary and moderate Harrison's groove, sternum projects forward at an increased angle, nipple line is very high.

Abdomen: "Pot-belly," liver palpable.

Spine: Marked rounded kyphos in the midlumbar region.

Lower Extremities: Short for length of trunk, abduction limited to 70 degrees, trochanters 2 cm. above Nélaton's line, moderate anterolateral bowing of the femora, slight lateral bowing of the tibiae, large amount of subcutaneous fat.

Neuromuscular: Child cannot walk or stand so far as is known, child leans forward when sitting, usually supporting the body by the hands resting on the knees.

Measurements.—See table.

Laboratory Examination.—Tests for tuberculosis and syphilis were negative.

Mental Examination.—Intelligence normal for age, although child seems to be both deaf and dumb.

CASE 3.—Frank B.: age, 4½ years; Swedish parentage.

Family History.—Negative for tuberculosis, rheumatism, joint diseases, central nervous system disturbances and venereal disease. Mother had one miscarriage and one still-birth before birth of this child. One other child living and well. No other deformities in the family.

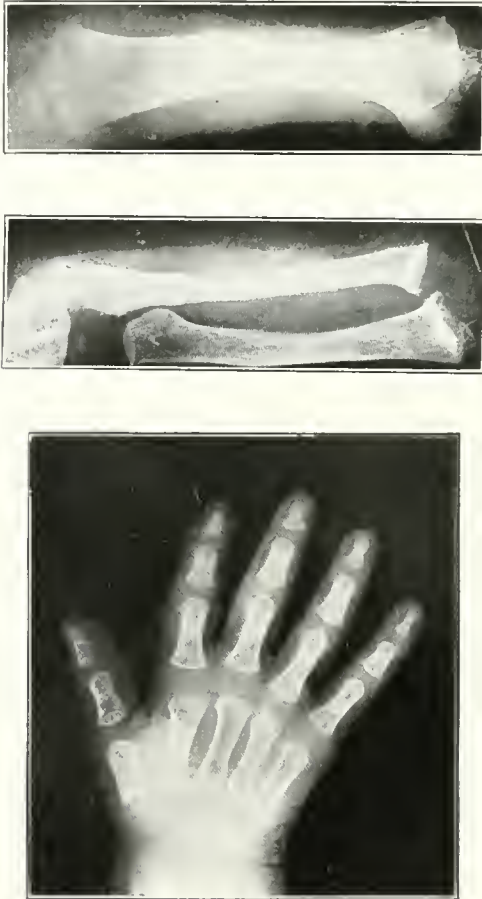


Fig. 7.—Ita P. Roentgenogram showing: (a) the short clubby humerus with evidence of an old fracture; (b) the short ulna and radius with flaring diaphyseal ends; (c) "main en trident"; (d) the short, thin bones of the hand.

Patient's History.—Full term, normal delivery. Weighed 12 pounds at birth. Mother noticed at birth that the bridge of the nose was very much sunken. There was some disproportion of trunk and extremities. Breast fed until 7 months of age and then given modified milk. Did fairly well. Measles at 1 year of age. Frequent colds in the nose and sometimes there was a bloody

discharge. Walked at 12 months of age. Talked late but is very bright for his age. Tonsils and adenoids removed at 3 years of age. Has frequent dislocation of left elbow joint.

Present Illness.—Mother brings child into hospital because of lack of growth, shortness of extremities, and dislocation of left elbow. Duration for life.

Physical Examination.—General: well developed and nourished boy with bright appearance.

Head: Large, prominent bosses, bulging forehead, anterior fontanel just closing, broad sunken nasal bridge, projecting ears.

Neck: Negative.

Upper Extremities: Short for length of trunk, marked epiphyseal enlargement, elbow shows slight limitation of motion, unable to extend forearm fully.

Chest: Negative, except for depression at ensiform and increased forward projection of the sternum.

Abdomen: Distended, otherwise negative.

Spine: Negative.

Measurements.—See table.

Laboratory Examination.—Tests for tuberculosis and syphilis were negative.

Mental Examination.—Intelligence normal for age.

CASE 4.—Dorothy A.; age, 6½ years; Irish parentage.

Family History.—Negative for tuberculosis, rheumatism, joint diseases, central nervous system disturbances and venereal disease. Two sisters living and well. No other deformity in the family.

Patient's History.—Full term, normal delivery. Birthweight, 8½ pounds. Breast fed for nine months. Measles at 2 years of age.

Present Illness.—Comes to hospital because of knock knees of one year's duration.

Physical Examination.—General: well developed and nourished girl.

Head: Negative.

Neck: Negative.

Upper Extremities: Short for length of trunk, hands are spade-like in shape with a scar where a sixth finger has been removed at the sixth metacarpophalangeal joint of each hand; all finger nails are under developed.

Chest: Negative.

Abdomen: Prominent and very long.

Spine: Six lumbar vertebrae.

Lower Extremities: Short for length of the trunk, double knock knee deformity; on the inner side of each tibia there is a nodule of bony hardness about one inch in diameter projecting from the bone at the upper epiphyseal line, there are six toes on each foot with syndactylism of the second and third.

Neuromuscular: No disturbances.

Measurements.—See table.

Laboratory Examination.—Tests for tuberculosis and syphilis were negative.

Mental Examination.—Intelligence normal for age.

CASE 5.—Beatrice R.; age, 9½ years; Irish parentage.

Family History.—Negative for tuberculosis, rheumatism, joint diseases, central nervous system disturbances and venereal disease. One brother living and well. Mother had one miscarriage at fourth pregnancy from unknown cause. Two brothers dead of "cholera infantum" and one dead of convulsions at 6 months. No other deformities in the family.

Patient's History.—Full term, instrumental delivery, birth weight 5 pounds. Breast fed for one year. Pneumonia and relapse at 2 years of age. Pertussis

at 3 years of age. Measles and pneumonia at 7 years of age. Chickenpox and bronchitis at 8 years of age. Constipated most of the time.

Present Illness.—Brought to hospital because of knock-knees of three years' duration. Mother says child was queer even at birth.

Physical Examination.—General; well developed and well nourished girl.

Head: fairly large and square; forehead prominent and well marked frontal bosses; poor teeth which are notched; slight prognathia; hoarse voice.

Neck: negative except rather short.

Upper extremities: humeri are short and thick; carrying angle is much exaggerated; hands are short, fat and thick; fingers are short and there is an increase of space between the index and middle fingers of both hands; the finger nails are thick and resemble horn; the left hand shows a linear scar where a sixth finger has been removed.

Chest: flat and narrow, flaring of lower ribs and Harrison's groove, irregular shortened clavicles.

Abdomen: protuberant.

Spine: negative.

Lower extremities: short for length of the trunk; excessive knock-knees; enlarged ends of the diaphyses at the ankles; feet are very short; great toes are normal in length but the four small toes on both sides give the appearance of the bones being too short for the growth of the soft parts; all toe nails show horny overgrowths.

Neuromuscular: on standing, child has marked lordosis, walks with peculiar gait because of knock-knee deformity and flat feet.

Measurements.—See table.

Laboratory Examination.—Tests for tuberculosis and syphilis were negative.

Mental Examination.—Child very intelligent for age.

CASE 6.—Basiliki S.; age, 10 years; Greek parentage.

Family History.—Negative for tuberculosis, rheumatism, joint diseases, central nervous system disturbances and venereal disease. Four other children living and well. No other deformities in the family.

Patient's History.—Full term. Normal delivery. Birth weight, 12 pounds. Breast fed for one year. Has had no illness.

Present Illness.—Mother brings child to hospital because she does not grow large like her other children.

Physical Examination.—General; poorly developed but well nourished girl.

Head: large and square with prominent forehead and bosses; nasal bridge sunken; cretinistic facies.

Neck: rather short.

Upper extremities: very short for length of trunk, marked epiphyseal enlargement.

Chest: moderate rosary and Harrison's groove, nipple line is very high and angle of sternum increased so that sternum projects almost horizontally.

Abdomen: tendency to "pot-belly."

Spine: negative except for lordosis on standing.

Lower extremities: too short for length of trunk; marked epiphyseal enlargement; rather too much subcutaneous fat.

Neuromuscular: negative.

Measurements.—See table.

Laboratory Examination.—Tests for tuberculosis and syphilis were negative.

Mental Examination.—Intelligence normal for age.

TABLE 1.—COMPARING MEASUREMENTS OF ACHONDROPLASTS WITH THE MEASUREMENTS OF NORMAL CHILDREN

	Age, Years	Weight, Lbs.	Circum- ference of Head, Cm.	Circum- ference of Thorax, Cm.	Height, Cm.	Length of Arm, Cm.	Length of Leg, Cm.
Emily S.	1 8/12	25 8/16	45.0	42.5	70.4	24.1	30.0
Normal 1*			48.0	48.0	35.0	33.0
Normal 2†		25 8/16	46.0	47.7	85.9	32.0	40.5
Ita P.	1 10/12	21 11/16	46.4	45.4	78.3	27.4	34.6
Normal 1.			46.4	45.4	28.0	36.5
Normal 2.		27 0/16	48.5	48.6	84.1	29.4	39.8
Frank B.	4 1/12	32 8/16	55.0	51.0	87.0	27.8	36.0
Normal 1.			49.9	50.9	30.8	41.5
Normal 2.		36 8/16	50.9	43.9	101.2	33.6	47.2
Dorothy A.	6 1/12	33 1/16	48.8	48.0	90.8	27.2	40.5
Normal 1.			49.9	50.5	36.0	50.5
Normal 2.		48 0/16	52.3	56.3	114.3	43.2	60.1
Beatrice R.	9 8/12	67 0/16	51.2	62.1	121.7	43.0	57.0
Normal 1.			54.0	63.0	46.6	65.0
Normal 2.		67 0/16	52.0	60.2	134.7	49.5	74.1
Basiliki S.	10	67 0/16	56.2	61.3	107.0	38.8	52.3
Normal 1.			54.0	63.0	40.0	55.0
Normal 2.		67 14/16	52.7	62.4	135.7	49.7	74.9

* Normal 1—When compared to children of same weight and height.

† Normal 2—When compared to children of same age.

The foregoing cases illustrate so well the symptoms of dwarf growth and infolding that each will not be taken up in detail here. A complete discussion of the symptoms will be found in connection with the plates at the end of the paper. At this time we wish to mention only a few of the more salient features.

GROUPING OF CASES

1. We seem to have two groups of cases:

A. That including Dorothy A., Beatrice R. and Basiliki S. shows more the symptoms of dwarf growth, while

B. That including Emily S. and Ita P. shows the symptoms of infolding.

Frank B. falls between these two groups, having symptoms of each.

2. Emily S. and Ita P. have a feature which seems hitherto undescribed, for we can find no mention of it in the literature.

Each case has an arcuate kyphos with a point of greatest convexity. Emily S. has this in the dorsal region, while in Ita P. it is dorsolumbar.

Roentgen-ray examination of this region shows a wedge-shaped vertebra at the point of greatest convexity.

Since there is no disease of the spine in either of these cases, we have taken the stand that this peculiar vertebra is the result of Jansen's "amnio pressure." The same force which presses on the two ends of the spine producing the kyphos might also very easily, it seems to me, produce this wedge-shaped vertebra.

3. Dorothy A. and Beatrice R. have in addition to the ordinary symptoms of "achondroplasia" certain bony changes which can easily be seen in the roentgenograms. Because of the limitation of time, it

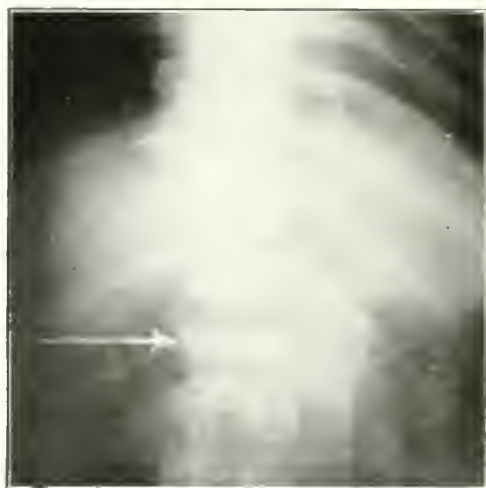


Fig. 8.—Ita P. Roentgenogram showing the wedge shaped vertebra; antero-posterior view.



Fig. 9.—Ita P. Roentgenogram showing lateral view of the wedge shaped vertebra.

has not been possible to work out this added complication, but it seems to me that some of the changes agree very well with those described by Ehrenfried (1915).

PATHOLOGIC CHANGES

Kaufmann (1892) described the pathologic condition in achondroplasia and on it based his three forms: (1) Chondrodystrophia hypoplastica; (2) chondrodystrophia malacica; (3) chondrodystrophia hyperplastica. In the first, he described a simple cessation in the growth of the cartilage; in the second, an arrest of the growth depending on the softening of the cartilage, and in the third, not simply an arrest of the growth of the cartilage, but an excessive growth, abnormal in its direction.

Morse (1902) says: "The most important pathologic process is, in brief, a disturbance of the normal process of ossification of the primary cartilage." He reviews Kaufmann's article and adds "Osteo-



Fig. 10.—Ita P. Roentgenogram showing the poorly developed pelvis

porosis and osteosclerosis may occur as complications in any case. Fractures may also increase the deformities."

Bullard and George (1908) review the work of Apert (1901) and Durante (1902) and have the following résumé: "Sclerosis of the epiphyseal cartilage while in preparation for multiplication. Lack of serial arrangement of the cartilage cells and deficiency in cartilaginous ossification while processes from the marrow cross the line of ossification. Abundant periosteal ossification produced as well by means of osteoblasts as by direct calcification of the fibrous lamellae, but only eventuating in the formation of a spongy bone with thick resistant lamellae. Sclerosis of the bone marrow."

Jansen (1912) says the ossification of the epiphyses is very much retarded, while the diaphyses, on the contrary, have not only formed

relatively more bone, but the edges of the periosteal bone have grown round the epiphysis in the shape of a funnel. The periosteum often forms a process (Kaufmann) which penetrates between the diaphyses and epiphyses, and Wallaardt Sacré finds the periosteum of long bones showing a more rapid growth at their ends, so that the diaphyses surround the epiphyses very nearly like "cuffs." "All this," he says, "proves that the periosteal bone grows faster than the epiphyseal. The periosteal bone is not completed by the addition of endochondral bone, which the epiphysis normally deposits at the ends of the diaphysis. The epiphysis is at fault, but still the periosteum continues its growth sometimes in the normal direction, forming a funnel around the epiphysis, or sometimes, departing from the right track by separating diaphysis and epiphysis by an abnormal layer of cellular tissue."

"The microscopic picture," Jansen adds, basing his opinion on the work of Kaufmann and Wallaardt Sacré, "of the achondroplastic bones confirms the opinion that in them the specific power of growth is diminished; the chief histologic characteristics of length growth in bone substance is constantly at fault; the columns of cartilage cells are too short, show irregularities in their arrangement and in their direction, or are lacking altogether." He does not pass on any decision as to how normally the cartilage cells are so thoroughly informed both of the direction of muscle action and of gravity, as to arrange their columns so precisely in these directions, but adds: "However that may be, the columns of cartilage cells in achondroplastic bones are situated less precisely in the long axes of the bones than normally. Moreover, they are shorter. Thus, the microscope reveals the picture of a diminution of the growth and the power of growth in achondroplastic bone."

I have not had the opportunity to study achondroplastic bone histologically. The work of others, probably due to lack of material, although describing single stages amply, does not at all exhaust the fields of embryological development of such bone. Such a piece of work would be valuable to consider in view of Jansen's work on the cause of achondroplasia.

THE ROENTGEN-RAY EXAMINATION

Most writers say little of the examination of cases of achondroplasia by the roentgen-ray method. Bullard and George (1908) has described it more fully. They divide the cases into two groups: (1) Those cases which are seen up to puberty without marked deformity; (2) cases with marked deformities of the limbs, or those cases in which there is a secondary joints lesion apparent (Kaufmann, 1892).



Fig. 11.—Ita P. Roentgenogram showing (a) the short bones of the lower extremities and (b) a definite tendency for the periosteum of the distal end of the femoral diaphyses to form a "cuff" about the epiphyses.

They say, "In the first group of cases the typical roentgen-ray picture of a given bone, the tibia for instance, will show it to be shorter and wider than that of a normal child, having a well developed ossific center for that given age. The shadow produced by the bone generally compares well with that of a normal child. Deformities of the shaft, with the exception of bowing, are rare in this group. The cortex is thicker, particularly in the middle of the shaft, showing considerable deposit of bone and thinning out toward the epiphyses. At the same time, the medulla, though small at the middle of the shaft, is increased in width proportionately with the thinning of the cortex; the bone structure in some cases is practically normal as compared with that of a normal child, but in the majority of cases a coarser and sometimes a more irregular deposit is apparent, particularly in the diaphyses.

"The most characteristic appearance of a long bone under examination in achondroplasia is that near the epiphyseal ends, the diaphyses become cup shaped, producing a T-shaped outline without any disturbance of the epiphyseal line or zone of proliferation, though they may be uneven and take on more or less fantastic shapes as compared with those of a normal individual. They are not, however, as uneven as in the diseases of nutrition, such as rachitis, where there is a definite disturbance of the zone of proliferation, but, as has been stated, the ossific centers have been well formed and the epiphyses are apparently fitted into the cup-like diaphyseal ends. In this first group of cases there is nothing seen in the roentgenograms which could be confused with rachitis.

"The second group of cases which we meet with in a large clinic is characterized by the large rectilinear head, extremities extraordinarily shortened in comparison to the bodies, the upper arms and thighs shortened in comparison to the forearms and legs, but distinguished from group (1) in that the osseous system shows more definite pathological changes such as scoliosis, kyphosis and lordosis of the spine, coxa vara, genu valgum or varum, and ankylosis, partial or complete, of one or more joints, due either to a mechanical inhibition of joint motion or to pathologic changes within the joint.

"In the roentgen-ray examination of these cases, though the underlying appearance of the bone is that of group (1), we have a more definite change of the articular surfaces of the joints, or of the epiphyses in general, to such an extent that one would hardly identify the given joint; there is a great distortion of the bone generally, with a tremendous increase in the size of certain portions, such as the great trochanter of the femur. The joint surfaces are practically absent, with a partial or complete erosion.

"It is to be noted that the epiphyses in this case are all delayed in their development, particularly as these children approach puberty, when there seems to be very little, if any, development of the epiphyses beyond a certain point."



Fig. 12.—Frank B. Aged 4½ years. Total length 87 cm.

In speaking of the roentgen-ray examination of long bones in which Bullard and George (1908) say the epiphyseal ends of the diaphyses have a "T-shaped" outline, Jansen (1912) refers to this as a "cuff" of periosteal bone and says that the roentgen rays show that the peri-

osteum forms more bone than the epiphysis. Kaufmann (1902) and Jansen (1912) contradict the statement of Bullard and George (1908) that there is not any disturbance of the epiphyseal line or zone of proliferation. They hold with others that there is a growth of fibrous tissue from the periosteum between the epiphysis and diaphysis.

THE CAUSE OF ACHONDROPLASIA

Morse (1902) said, "Little is known as to the cause of this disease." Such a state existed until 1912 when Jansen advanced his hypothesis that the amnion is the cause. His argument is so convincing that I review it here, first giving his summary of the various opinions of other writers on the subject.

He says: "Parrot (1878) who first recognized the affection as a separate entity, and introduced the name achondroplasia, considered it to be the nature of a congenital nutritive disturbance of the cartilage germ cells. Parrot thereby provided us with a circumlocation rather than an explanation of the facts.

"De Buck and Mayet (1900 and 1901) consider this change in cartilage germ cells as a sign of degeneration and consider the achondroplasts as the last member of a pedigree of degenerates." We may plead against this theory that achondroplastic women not frequently bear normal children (Treub, 1904).

Poncet and Leriche and others consider the achondroplasts as a separate race on account of the striking resemblance they show one to another. Against this it has been argued that, on account of the considerable narrowing of the pelvis, natural (Nolen) birth is usually impossible and thus the conditions necessary for the existence of a race as such are not met with. And even those who cling to the idea of a separate race, will feel the need of finding the causes which lead to this change.

"Bohn and Schwob (1868) deem a disturbance or insufficiency of the placenta probable in correlation with the nutritive disturbance." No facts have yet been brought forward in support of this suggestion.

"Klebs (1889) is of the opinion that the umbilical vesicle by an excessive development and a broadening of its stalk is able to compress the limb buds just after their formation, and so to stunt their growth." Even those who firmly believe in the correctness of this hypothesis must seek a further explanation for the changes in the skull.

"V. Franke (1893) and Rindfleisch (1899) have suggested that mechanical pressure of the surrounding tissues on the embryo might be the cause; but the hypothesis has been rejected on account of the symmetry of the dwarf growth in achondroplasia and the strong resemblance of every two cases, both of which characteristics dis-

tinguish it from the asymmetry and diversity shown by deformities known to be the result of external pressure (Sumita).

“Wissermann (Sumita) considers tightness or rather lack of expansion of the skin as a possible cause of the stunting in growth of the



Fig. 13.—Dorothy A. Aged $6\frac{1}{2}$ years. Total length 90.8 cm. This picture shows the short extremities and the extra toes

bones; but as has rightly been objected, the skin is not lacking in expansion in achondroplasia; on the contrary, its growth is relatively excessive so as even to lie in folds.

"Most of the authors who have written on achondroplasia consider it to be an hereditary infection or intoxication.

"Dor (1893) considers the toxi-infectious agent to affect the cartilage directly: typhoid fever promotes the growth of the skeleton, he argues; whilst on the other hand intestinal infections inhibit its growth. In the latter sense the unknown agent works from an early stage in the development of the skeleton.

"Syphilis and tuberculosis, alcohol and tobacco, the causal agents to which so many ills are attributed, have naturally not escaped being accused, each and all, of being responsible for this affliction; but again, no valid evidence has been brought forward in support of the accusation.

"Cestan (1901) and Reignault speak of intrauterine rickets."—Both in rickets and achondroplasia, indeed, shortening of the extremities occurs. In rickets, however, the disproportion is chiefly due to curvature of the bones; in achondroplasia it depends on their insufficient growth in length. Moreover, an achondroplast is born as such and remains so for life. Rickets, on the contrary, appears after birth and disappears later on in life. To label the two affections with one name would, therefore, create confusion rather than afford a deeper view into the nature of either.

"Porak and Durante (1905) base their opinion on the histological appearance of achondroplastic cartilage. They consider it to be characterized by sclerosis. All substances that exercise a sclerogenetic influence on cartilage may—according to them—be the cause of achondroplasia. New data afterward led them to the conviction that in addition to the theory of hereditary infection or intoxication, which they postulate as a casual agent, certain forms of achondroplasia might be brought about by autointoxication." We doubt whether the insight which the histological aspect of this affection affords, is explicit enough to justify such far reaching conclusions.

"P. Marie expresses himself with more caution: Could there not in this disturbance of development, be something analogous to myxedema; should we not seek the cause of achondroplasia in a deficiency in the function or the development of some gland?

"All glands with internal secretion have indeed been suspected in the attempt to answer this question:

"Leblanc (1902), who found myxedema and achondroplasia combined in a calf, considered the thyroid gland responsible.

"Lugaro also saw the two affections combined in man, and Devay (Parhon, Shunda and Zalplachta, 1905) as well as Collmann, on the contrary, found the thyroid gland enlarged in a case of achondroplasia. In by far the majority of achondroplasts this gland is normally

developed. Identifying the two affections would mean returning to the old standpoint of Virchow who confused achondroplasia and cretinism. Clinicians have since placed the two wide apart. Yet, the relative frequent coincidence of these two affections raises the suggestion that the causes of congenital cretinism and achondroplasia may be related.

"Vargas raises the question, whether the thymus may be the cause; but without procuring any support for this hypothesis.

"Parhon, Shunda and Zalplachta (1905) consider it possible that a hypofunction of the pituitary body, the thyroid gland and the thymus, combined with a hyperfunction of the sexual glands might produce achondroplasia. They strongly emphasize the latter. Before birth this enhanced action of the genital glands might be excited by the ovaries of the mother, and after birth the child's genital glands



Fig. 14.—Dorothy A. This picture shows the extra toes, the second and third being webbed, and the horny irregular toenails.

might begin to exert their influence too early and too powerfully. Especially after the publication of Leriche's (1904) observations, they strongly inclined toward the great influence of the latter, of which Leriche says: 'au rebours du gigantisme avec lequel elle (—la glande interstitielle du testicule et de l'ovaire) est en relation manifeste en certains cas par défaut, la glande testiculaire pourrait peut-être par viciation ou par excès produire un arrêt de croissance.' It is especially the experiments of Leriche's teacher, Poncet, and those of Dor and Maisonave which served as the foundation of his belief. The former, indeed, has ascertained that castration causes excessive growth of the skeleton, while the latter elicited a "sterilization relative" of the diaphyso-epiphyseal cartilage discs and a stunting in the growth of animals in injecting extract of testicle. However, these experiments

have not led to achondroplasia by any means; and it would thus be premature to consider achondroplasia as the effect of an exaggerated secretion of the sexual glands both of the mother (before parturition) and of the child (soon after birth). Moreover, the enlargement of the skeleton by castration is greatly exceeded by gigantism; and the effects of gigantism and castration are not to be identified.



Fig. 15.—Dorothy A. Roentgenograms showing (a) the extra metacarpals and metatarsals, the extra fingers having been removed at operation, the extra toes being present; (b) the character of the metacarpal and metatarsal bones and (c) the epiphyses surrounded by periosteal "cuffs."

"Ettore Levi (1909), to complete this enumeration of writers, rejects the hypothesis of P. Marie—and in our opinion—he is quite

right in so doing; Levi is ready to admit that gigantism may be caused by a disturbance in the function of a blood gland, and even infantilism, because in these affections all segments of the skeleton are modified. In achondroplasia, however, we cannot see how a blood gland could



Fig. 16.—Beatrice R. Aged $9\frac{8}{12}$ years. Total length 121.7 cm.

be the cause, because the dystrophy is restricted chiefly to the extremities.

"In short, we find that the causes of achondroplasia are still completely enshrouded in obscurity; local nutritive disturbances in the

cartilage, infection—both hereditary and direct—intoxication—both exogenic and endogenic—sclerogenetic influences, race peculiarities, degeneration, defective function of glands, mechanical pressure—form the motley series of possibilities from which science has hitherto been unable to make her choice.

"It will now be our task to find out whether the mechanical malformations, which characterize the achondroplast, and which we have proved to be the results of infolding of the fetus, may put us on the track of the causes of this disproportionate dwarfing of the growing body in achondroplasia."

Jansen says that the mechanical malformations, characteristic of achondroplasia, could be brought about by three compressing forces which act on the head, the neck and the tail bends of the embryo and, so to speak, roll it up in its long axis. He does not believe that this can be produced by direct pressure from maternal parts, because of the space between the amnion and the fetus. Nor does he believe that pressure on the fetus transmitted by the chorionic liquid could bring about the malformations because this pressure would be the same in all directions and be unable to accentuate the normal bends in the manner found characteristic of achondroplasia.

By exclusion, then, we must find in the amnion the source of the deforming forces. Only two conditions of this need be considered, i. e., hydramnion and smallness of the amnion. That hydramnion does not constantly bring about these malformations may be understood, when we consider (1) that rapid growth or distention of the amnion might soon put an end to the abnormally high pressure, and give the embryo an opportunity of resuming the normal attitude before injury has been inflicted; and (2) that, when the abnormal increase of liquid in the amniotic sac begins (only after the amnion has been lifted from the surface of the embryo) the abnormal axial pressure need not be exercised.

It then remains that, except in rare cases, the deforming forces must be due to the smallness of the amnion. That the amnion is often affected by such a primary disturbance in growth is accepted by such investigators as Dareste (1892), Marchand, Schwalbe, Kocher, von Volkmann and others.

But we have not considered the cause of the dwarf phenomena. If the smallness of the amnion produces the malformations of infolding, can the same cause affect the growth of the deep lying parts? This seems to be the case, and it takes place in the following way. The amnion which folds up the embryo, at the same time impedes the supply of food by producing a closer contact of the cells and a diminution of the nutritive fluids. If it may be accepted that embryos are

rolled up by their amnion, it is also certain that the direct amnion pressure has caused the preponderant axial dwarfing of the pelvis and in a lesser degree that of the spine. And that which is true of the direct amnion pressure in one direction, is true of the hydrostatic pressure in all directions; if the axial pressure of the amnion is able to squeeze blood out of the scleroblastematous spine in one direction, then the hydrostatic pressure is able to do the same in all directions. If a direct pressure of the amnion can cause dwarf phenomena in one direction, the indirect hydrostatic pressure can do the same in all directions; in other words, if direct amnion pressure is the cause of the phenomena of infolding in achondroplasia, then indirect or hydrostatic amnion pressure is the cause of the dwarf phenomena.



Fig. 17.—Beatrice R. Roentgenogram showing the misshapen fifth metacarpals where a sixth finger has been removed at operation, and the epiphyses of the phalanges surrounded by the peculiar funnel-shaped "cuff" of periosteal overgrowth.

In view of this we understand that the bones formed in cartilage are most affected because they increase their volume more rapidly than other tissues and because they demand such a large amount of nutrition in their growth. In other words, heightened amnion pressure, through a diminution of blood supply, leads to an "aplasia" of "chondrium," an "achondroplasia." And, the bones formed in membrane (except in the severest forms) pass unmolested because they are not gluttons.

Above all, it becomes clear why the growth disturbance affects the latest formations most, the earliest least, for each younger part of the skeleton forms its cartilage under more unfavorable conditions.

We can now see that the severest forms of achondroplasia must be produced by the smallness of the amnion, while the relatively slight

forms may have been produced by less damaging hydramnion. Further, Jansen (1912) believes that hare lip, micrognathy, apnathy, myxedema, hydrocephalus, gas bubbles in the internal organs, subcutaneous fatty masses and increased sexual function which are often found in the achondroplast, may be considered in relation to this same direct and indirect amnion pressure. His observations on the latter are especially interesting. Summing up his facts, we find in:

castrates:	sexual functions	< →	pituitary	>	growth	>	
pregnancy:	sexual functions	<	pituitary	>	growth	>	
acromegaly:	pituitary	>	growth	>	→	sexual functions	<
gigantism:	pituitary	>	growth	>	→	sexual functions	<
achondroplasia:	pituitary	<	(growth	<)	→	sexual functions	>

Thus the idea is suggested that the exaggeration of the sexual functions which we observe in achondroplasts may be the consequence of the disturbance in the development of the pituitary body which we found in the severer cases.

THE TIME AT WHICH THE CHANGES OF ACHONDROPLASIA TAKE PLACE

The question now quite naturally arises as to when this infolding of the embryo takes place. The following things strongly suggest the idea that the embryo, between the third and eighth week of its intra-uterine life, has been, so to speak, bent up, infolded, "coiled up" like an anchor rope:

(1) The degree of retardation of growth of the various parts of the skeleton is determined by the time of their primary formation from the scleroblastema, as can be seen in Table 2.

TABLE 2.—COMPARISON OF DATE OF FORMATION AND RATIO OF ANOMALIES.

A. Date of Formation (Keibel and Mall, 1910)				B. Ratio of Anomalies (Jansen, 1912)		
	Of the sclero-blastema	Of the cartilage	Of the centers of ossification		In smaller dwarf skeletons	In larger dwarf skeletons
Of the cervical vertebrae	3d week	5th week	56th day	Of the breadth of 3d cervical vertebra	$\frac{1}{1.97}$	$\frac{1}{1.31}$
Of the lumbar vertebrae	After the cervical vertebrae	5th week	73d 105th day	Of the breadth of 3d lumbar vertebra	$\frac{1}{3.10}$	$\frac{1}{1.5}$
Of the humerus diaphysis	End of 4th week	5th week	42d day	Of length of humerus diaphysis	$\frac{1}{3.63}$	$\frac{1}{2.5}$
Of the femur diaphysis	Early after humerus 5th week	5th week	42d day	Of length of femur diaphysis	$\frac{1}{3.47}$	$\frac{1}{2.80}$
Of the epiphysis	After diaphysis		10th month or after birth	Of the thickness of cartilage between femur and tibia diaphysis	$\frac{1}{8.33}$	$\frac{1}{3.00}$

Thus we see the formation of the primitive vertebrae starts in the cervical region and proceeds in a caudal direction; and it is only after the sacral vertebrae have been formed that the extremities bud. In these again the epiphyses are the latest formations. And in the same order we see the various parts of the skeleton in achondroplasts affected in a successively increasing measure.



Fig. 18.—Beatrice R. Roentgenogram showing the clubby shape of the femurs; the cortical thickening with resulting decrease in caliber of the medullary canal and the bowing of the femurs, especially the left.

2. It may be remembered that the pituitary body develops between the second and eighth weeks of fetal life and that its larger anterior part is formed by a diverticulum of the roof of the primitive mouth, which pierces the mesodermal covering of the brain vesicle between



Fig. 19.—Beatrice R. Roentgenogram showing: (a) the difference in length of the tibiae. The bowing of the left femur exactly compensates for the increased length of the left tibia for the lower extremities are of the same length; (b) the bulbous ends of the long bones; (c) the small exostoses which are present at the epiphyseal lines; (d) the cortical thickening of the bones and (e) the eccentric medullary canals.

the future presphenoid and postsphenoid, i. e., between the anterior and the middle bone centers of the tribasilar bone. Thus, the fact that the sella turcica may be totally absent, if indicating that the development of the pituitary body has been disturbed may suggest the inference that this disturbance has taken place between the second and eighth weeks of fetal life.

3. In order that the skull shall assume the form often seen in the foregoing discussion the change must have been brought about at a period of fetal life, when the skull was still membranous, either entirely or for the greater part.

4. From Table 2 we see that the scleroblastema formed at the third week begins to change into cartilage about the fifth week, while the formation of bone begins at about the eighth week. The suitable time, then, for the malformations of the spine lies between the third week, when the condensation of the primitive cellular tissue into scleroblastema may be observed, and the eighth week, when the cartilaginous formation begins to harden into bone substance.

5. The form of the normal embryo of 4 weeks is such that (a) pressure on the head curve must needs push the region of the visceral arches and the future face against the organs of the future chest and the chest wall. It is quite intelligible that this is the way in which the region of the future nose has been either partly or wholly flattened and the hard palate displaced in the direction of the base of the skull. Therefore, an accentuation of the normal neck curve subjects the parts of the future face to a compression which fully explains their characteristic malformation in achondroplasia. (b) Similarly, a pressure at the neck curve may have moved forward the parts of the squama occipitalis. It may have narrowed the foramen magnum, when its anterior border, the lower part of the tribasilar bone, was driven against a firm resistance (the hard palate in front), or have displaced it in a forward direction, i. e., kyphotized the base of the skull, when no such bony resistance was met with, the posterior border of the palate being tilted high up. (c) Finally, the forces at the caudal end of the fetus counteracted those acting on the head, and have kyphotized the spine.

6. If we believe the smallness of the amnion to be the cause of the mechanical malformation, the changes must take place between the third and eighth week, for it is during the third week that the amnion obtains the power of folding up the embryo. Up until then the amnion with its mesodermal and ectodermal layers is about as thick as the embryo and hardly inferior to it in firmness. During the sixth week

the amnion probably loses the power of folding up the embryo because the embryo rapidly increases in firmness and by the seventh and eighth week the skeleton finally presents ossification centers.

RESUME

1. The name "achondroplasia" has been chosen for the condition under discussion because the state is an "aplasia" of "chondrium."

2. Achondroplasia is characterized by symptoms of dwarf growth (shortness of extremities, vertebral column and chest and looseness of the skin) and symptoms of infolding (kyphosis baseos cranii, sagittal narrowing of the foramen magnum, depression of the nasal bridge, narrowing of the choanae, reduction in the size of the sella turcica with consequent reduction in the size of the pituitary body, and changes in the spine).

3. The changes of achondroplasia are probably due to the smallness of the amnion, except in rare cases.

4. The changes of achondroplasia are produced between the third and eighth weeks of intra-uterine life.

5. The pathologic changes consist mainly in a retardation of ossification of the epiphysis and the diminished production of endochondral bone, while the periosteum produces a comparatively normal amount of bone.

6. Besides the deformities of the bones, the characteristic roentgenologic appearance of a long bone under examination shows that near the epiphyseal ends the diaphyses become cup-shaped, producing a T-shaped outline without any disturbance of the epiphyseal line or zone of proliferation, though these may be uneven and take on more or less fantastic shapes as compared with those of a normal individual.

7. All the cases presented in this paper bear out all that has been said, and in addition two of them show a new symptom, a wedge-shaped vertebra, which falls in the group of symptoms of infolding, and fortifies the belief that the state of achondroplasia is produced by the smallness of the amnion.

BIBLIOGRAPHY

In arranging the bibliography, I have included all writers that we could find who have touched on achondroplasia or its problems. In some cases, writers have referred to the work of others without giving their source of information. I have included the names of the latter, after finding the original articles in all cases possible. I have not been able to locate a few, but the names of these have been given, in the hope that someone else, interested in this problem, may be more fortunate in finding them.

Apert: *Nouv. leçon. de la Salpêtrière* **14**: 1901.

Aschner: *Verhandl. d. deutsch. Gesellsch. f. Chir.*, 1910.

Ashhurst: *Ann. Surg.* **63**:167 (Feb.) 1916.

- Austregesito and Esposel: *Brazil méd.* **28**: (April) 1914.
- Ballantyne: *Keating's Cyclopedia of Diseases of Children*. Supplement.
- Benda: *Deutsch. klin. am Eingang d. 20. Jahrh.* **3**: 1903.
- Bertolotti: *Presse méd.* **21**: (June 28) 1913.
- Bertolotti: *Semana méd.* **21**: (Jan. 8) 1914.
- Bertolotti: *Riforma méd.* **31**: (Feb. 6) 1915, No. 6.
- Bircher: *Lubarsch and Ostertag, Ergebnisse*, Part 1, 1896.
- Boeckh: *Arch. f. Gynäk.* **43**: 1893.
- Bohn: *Jahrb. f. Kinderh.*, 1868.
- Bolk: *Geneeskunige Bladen* **9**: 1906.
- Bouchard and Brissaud: *Traité de Médecine*, 1905.
- Bradford and Lovett: *Textbook of Orthopedic Surgery*, 1915.
- Brissaud: See Bouchard and Brissaud, 1905.
- Bullard and George: *Boston M. & S. J.* **158**: (June 25) 1908.
- Bychowsky: *Deutsch. med. Wchnschr.*, 1909.
- Cestan: *Nouv. Iconogr. de la Salpêtrière*, 1901.
- Charpentiere: *Arch. de Toxicol.*, 1876.
- Chevalier: *Iconogr.*, No. 3, 1910.
- Clopatt: *Finsk. Läk.-Sälls. Handlingar* **57**.
- Collmann: Original reference not found. Referred to by Jansen (1912).
- Crimail: *Ann. de Gynécol.*, 1889.
- Dareste: *Compt. rend. Acad. d. sc.*, Jan. 23, 1882.
- Dareste: *J. de l'anat. et de la Physiol.*, 1882.
- De Bück and Mayet: *Belgique méd.*, 1900.
- De Bück and Mayet: *Rev. neurol.*, 1901.
- De Paul: *Arch. d. tocol.*, 1877.
- De Paul: *Arch. d. tocol.*, 1878.
- Devay: See Parrhon, Shunda and Zalplachta, 1905.
- Dixon: *Brit. M. J.*, Sept. 11, 1909.
- Dor: *Eighth Congr. d. chir.*, 1893.
- Durante: *Rev. méd. de la Suisse Rom.* **22**: 1902.
- Durante: See Porak and Durante, 1905.
- Dufour: *Nouv. Iconogr. de la Salpêtrière*, No. 2, 1906.
- Edgeworth: *Bristol M.-Chir. J.* **17**: 1899.
- Ehrenfried: *J. A. M. A.* **64**: 1640 (May 15) 1915.
- Ehrenfried: *Am. J. Orth. Surg.* **15**: 463 (June) 1917.
- Eicholz: *Brit. M. J.* **1**: (May 21) 1910.
- Esposel: See Austregesito and Esposel, 1914.
- Fédé and Finizio: *Rev. mens. d. mal de l'enf.* **19**: 1901.
- Feyerabend: *Inaug. Dissertation*, Königsberg, 1890.
- Finkelstein: *Lehrb. d. Kinderkrankheiten*.
- Finizio: See Fédé and Finizio, 1901.
- Franqué: *Sitzungsberichte de Phys.-Med. Gesellsch. z. Würzburg*, 1893.
- Friedenheim: *Inaug. Dissertation*, Berlin, 1894.
- Fussel and Paucoast: *Penna. M. J.* (July) 1910.
- Gegenbaur: *Anatomie*, Ed. 7, Pt. 1.
- Gemelli: *Folia biol.* **2**: 1908.
- George: See Bullard and George, 1908.
- Gould and Pyle: See Thomson, 1893.
- Grover: *Arch. Pediat.*, June, 1915.
- Hart: *Edinburgh M. J.* **10**: (June) 1913.
- Hildebrand: *München. med. Wchnschr.* **46**: 1899.
- Hirst: *Med. News* **64**: 1894.
- Iis: *Anatomie menschlicher Embryonen* **2**.
- Jansen: *Achondroplasia*, Leyden, 1912.
- Jansen: *Ztschr. f. orthop. Chir.* **32**: 1913.
- Joachimsthal: *Deutsch. med. Wchnschr.* **25**: 1890.

- Joachimsthal: Handbuch d. orthop. Chir. **2**.
 Johannessen: Beitr. z. path. Anat. **23**: 1898.
 Kaufmann: Untersuchungen u. d. sogenannte fötale Rachitis, Berlin, 1892.
 See Marchand's Review.
 Kaufmann: Centralbl. f. allg. Path. u. path. Anat. **4**: 1893.
 Kassowitz: Die norm. Ossification u. die Erk. v. des Knochensystems bei Rach. u. hered. Syph. **2**: 1885.
 Keibel and Mall: Handbuch der Entwicklungsgeschichte des Menschen, 1910.
 Keith: Lancet **1**: (April 15) 1911.
 Klaussner: Ueber Missbildungen der menschlichen Gliedmassen und ihre Entstehungsweise. Wiesbaden. 1900.
 Klebs: Allgemeine Pathologie, 1889.
 Kocher: Deutsch. Ztschr. f. Chir. **9**.
 Kocher: Deutsch. Ztschr. f. Chir. **100**: 1909.
 Kollmann: Lehrb. der Entwicklungsgeschichte des Menschen, 1893.
 Kuh: Ztschr. f. orthop. Chir. **29**: 1911.
 Lampe: Inaug. Dissertation, Marburg, 1895.
 Langelann: Handelingen van het XII. Nederlandsch Natuur en Geneeskunig Congrès, 1909.
 Lauro: Arch. di Pathol. Int., September, 1887.
 Leblanc: Société des sc. vétérin, Lyon, 1902.
 Leriche: Gaz. d. hôp., February, 1904.
 Levi: Nouv. Iconogr. de la Salpet., 1909.
 Lovett: See Bradford and Lovett, 1915.
 Lugaro: Sul cretinismo sporadico.
 MacCallum: Bull. Johns Hopkins Hosp. **26**: (May) 1915.
 Maisonneuve: Original reference not found. Referred to by Jansen, 1912.
 Mall: See Keibel and Mall, 1910.
 Mason: Arch. Pediat. **11**: 1894.
 Massalongo and Piazza: Riforma med. **30**: (June 27) 1914.
 Mayet: See De Bück and Mayet, 1900.
 Moffett: New York M. J. **102**: (Sept. 11) 1915.
 Morse: Arch. Pediat., August, 1902.
 Müller: München. med. Abhandl., 1893.
 Nathan: Am. J. M. Sc., April, 1908.
 Nolen: Klinische Voordrachten.
 Osler: Trans. Am. Phys. and Surg. **4**: 1897.
 Palmegiani: Pediatria **23**: (Jan.) 1915.
 Pancoast: See Fussel and Pancoast, 1910.
 Parhon, Shunde and Zalplachta: Iconogr., 1905.
 Parrot: Bull. d. anthrop. de Par. **1**: 1878.
 Piazza: See Massalongo and Piazza, 1914.
 Pirrung: Lancet-Clinic **113**: (May 1) 1915.
 Pleyte: Chapitres supplémentaires du Liore des Morts, Traduction et commentaire, Leyden, 162, 162*, 163.
 Poncet: Original reference not found. Referred to by Jansen, 1912.
 Porak: De l'Achondroplasia, Clermont, 1890.
 Porak and Durante: Iconogr. de la Salpêtrière, 1905.
 Proust: J. de Chir., T. I.
 Pyle: See Gould and Pyle, 1893.
 Reignault: Original reference not found. Referred to by Jansen, 1912.
 Rindfleisch: Festschr. d. physik. med. Gesellsch. zu Würzburg, 1899.
 Roos: Ztschr. f. klin. Med. **48**.
 Salvetti: Beitr. z. path. Anat. **16**: 1894.
 Safford: Arch. Pediat. **1**: 1896.
 Sammies: Arch. Pediatrics **33**: 755 (Oct.) 1916.

- Schenk: Inaug. Thes. Rev. in Rev. d'Orth., 1911.
Schorr: a. d. Grenzgeb. der Med. u. Chir. **25**: 1912.
Schirmer: Centralbl. f. d. Grenzgeb. Med. u. Chir., 1907.
Schwalbe: Die Morphologie der Missbildungen, Pt. 1.
Schwalbe: Die Morphologie der Missbildungen, Pt. 3.
Shunda: See Parhon, Shunda and Zalplachta, 1905.
Slingenberg: Original reference not found. Referred to by Jansen, 1912.
Smith: Am. Textbook Dis. Child., 1894.
Smith: Dis. Child., 1896.
Smith, G. Elliot: Introduction to Jansen, 1912.
Smith, W. A.: J. S. Carolina M. A. **11**: (March) 1915.
Stoeltzner: Jahrb. f. Kinderh. **50**: 1899.
Sumita: Deutsch. Ztschr. f. Chir. **107**: 1911.
Symington and Thompson: Proc. Roy. Soc. Edinburgh **18**: 1890-1891.
Symmers and Wallace: Arch. Int. Med. **12**: 742 (July 15) 1913.
Swoboda: Original reference not found. Referred to by Jansen, 1912.
Tamburini: Ric. sperim. de fren. **20**: 1894.
Thomson: Edinburgh M. J. **38**: 1893.
Thompson: See Symington and Thompson, 1890-1891.
Townsend: Arch. Pediat. **11**: 1894.
Treub: Bull. Soc. d'obst., February, 1904.
Tschistowitch: Arch. Russ. d. Pathol., October, 1896.
Unruh: Wien. med. Bl.
Vaglio: Pediatria **23**: (July) 1915.
Virchow: Original reference not found. Referred to by Jansen, 1912.
Vrolik: See Ballantyne.
Wagner: Arch. f. Gynäk. **100**: 1913.
Wallace: See Symmers and Wallace, 1913.
Weissermann: Arch. f. Entwicklungsmechanik d. Organismen **26**: 1909.
Whitman: Textbook of Orth. Surg., 1917.
Zalplachta: See Parhon, Shunda and Zalplachta, 1905.

THE FOOD VALUE OF THE MILK OF THE WATER BUFFALO

WILLIAM W. CADBURY, M.D.

Canton Christian College

CANTON, CHINA

If at one stroke all dairy products were rendered inaccessible to the people of the United States, it would be considered one of the greatest calamities that could befall the country and probably thousands of children would die of starvation. Yet this is the very condition that has prevailed in China for many centuries. Even at the present time, fresh butter, milk and cheese are rarely used by the Chinese people, and canned milk has been introduced into the more modernized districts only within the last two or three decades. This is the more remarkable, because next to the hog the cow is the commonest of domestic animals, at least in South China.

In view of these facts one is often amazed to observe that children can grow strong without milk, and that tuberculosis of the forms generally considered as bovine in origin may be very prevalent among a people who eat neither beef, butter nor milk. Rachitis is practically never seen. Nevertheless, I would be the last one to depreciate the great value of dairy products as a food, and it is undoubtedly because of their absence that thousands of China's babies die yearly. When an infant is weaned he is given congee, or rice gruel, and before he is a year old the mother begins to feed him with rice—which is to be the staple of his diet as long as he lives.

At the present time tinned milks may be obtained by most of the people in South China, but the fresh product is quite out of their reach. Dairies have recently been opened in Canton, but their products are often so unreliable that one hesitates to prescribe fresh milk to his patients. Because of this difficulty in obtaining a reliable milk a dairy has been established at the Canton Christian College where both buffalo and European cows are kept. The latter consist of modern breeds of cattle or their offspring imported from Australia, England or America. These cattle are expensive, are liable to succumb to disease, and it is not likely that they will ever become fully adapted to the climate of South China.

If China, then, is to have her own herds one should endeavor to select the cows from native stock. With this end in view, the agricultural department of the Canton Christian College has taken up the study of the milk of the carabao (*Bubalis Babalis*) or water buffalo.

These animals have long been domesticated by the Chinese farmers and take the place of the horse for ploughing the rice fields in the South. Their milk has never been used to any extent as a food, and no breeding experiments have been attempted in this direction.

Recently Mr. C. O. Levine,¹ instructor in animal husbandry at the Canton Christian College, has undertaken a careful analysis of the milk of the buffalo cows composing the herd kept at the college dairy. The samples for the analyses were taken directly from the cows in the barn and not from bottled milk on sale in Canton, which is frequently diluted with water.

TABLE 1.—COMPARATIVE PERCENTAGE COMPOSITION OF AMERICAN COW'S MILK AND WATER BUFFALO MILK

	Buffalo Milk, per Cent.	American Cow's Milk, per Cent.
Fat.....	12.60	3.69
Proteids.....	6.04	3.53
Sugar.....	3.70	4.88
Ash.....	0.86	0.73
Water.....	76.80	87.17

The most noticeable fact in Table 1 is the marked excess of fat in water buffalo. The average of 12.6 per cent. was the result obtained from frequent analyses of thirty different cows over a period of eighteen months. The lowest average for any individual cow was 11.50 per cent, and the highest was 15.60 per cent. fat. While the fat is almost four times as much as that in the average American cow's milk, the proteid is almost twice as much; the sugar and water are less.

Buffalo milk is wholesome and palatable when produced under sanitary conditions. There is little or no odor. The strong disagreeable odor sometimes noted in buffalo milk is due largely to dead scales and hair from the body of the cow that have fallen into the milk during milking. One small flake of skin or one hair may taint a gallon of milk so that the flavor will be unpleasant. When milk is produced under sanitary conditions it may have an odor when first drawn. This is due to gases in the milk which leave it after the milk has stood for a short time in a clean, well ventilated room.

Undiluted buffalo milk commands a slightly higher price than the European cow's milk, because a buffalo cow produces a less quantity. It is probable that by careful breeding cows can be produced which will furnish as much milk as the average American herd.

1. Levine, C. O., and Cadbury, William W.: A Study of Milk Produced in Kwangtung, China M. I. 32:536, 1918.

On the other hand, the richer content in fat makes the milk more valuable. I supply my patients at the Canton Hospital with water buffalo milk from the Canton Christian College dairy. Half the quantity required is ordered and diluted with equal parts of boiled water. The patients are thus provided with a milk averaging 6.30 per cent.

TABLE 2.—WATER BUFFALO MILK FORMULAS FOR INFANTS

Age of Child	Water Buffalo Milk Mixture	Resulting Milk Formula Buffalo Milk, per Cent.			Correct Formula According to Holt, per Cent.		
		Fat	Sugar	Proteid	Fat	Sugar	Proteid
Premature Infant	Milk 20.0 Sugar 11.3 Water add 300.0	0.84	4	0.4	1.0	4	0.25
1st to 4th day	Milk 20.0 Sugar 14.3 Water add 300.0	0.84	5	0.4	1.0	5	0.3
5th to 7th day	Milk 25.0 Sugar 14.1 Water add 300.0	1.05	5	0.5	1.5	5	0.5
2d week	Milk 30.0 Sugar 16.9 Water add 300.0	1.29	6	0.6	2.0	6	0.6
3d week	Milk 50.0 Sugar 16.2 Water add 300.0	2.1	6	1.0	2.5	6	0.8
5th to 8th week	Milk 60.0 Sugar 15.8 Water add 300.0	2.5	6	1.2	3.0	6	1.0
3d month	Milk 70.0 Sugar 15.4 Water add 300.0	2.9	6	1.4	3.0	6	1.25
4th month	Milk 80.0 Sugar 18.0 Water add 300.0	3.4	7	1.6	3.5	7	1.5
5th month	Milk 90.0 Sugar 17.5 Water add 300.0	3.8	7	1.8	3.5	7	1.75
6th to 10th month	Milk 100.0 Sugar 18.0 Water add 300.0	4.2	7.2	2.0	4.0	7	2.0
11th month	Milk 100.0 Sugar 12.0 Water add 300.0	4.2	5.2	2.0	4.0	5	2.5
12th month	Milk 120.0 Sugar 11.0 Water add 300.0	5.0	5.1	2.4	4.0	5	3.0
13th month	Milk 150.0 Sugar 9.0 Water add 300.0	6.3	4.8	3.0	4.0	4.5	3.0

fat, 3.01 per cent. proteid and 1.85 per cent. sugar at a cost of between 4 and 5 cents, silver currency, for 200 mil. For children and adults it is always best to dilute the milk. It is especially convenient in feeding infants, and I generally prescribe it for infants less than one year of age in preference to the European cow's milk. I have given it to my own child, one year old, with great satisfaction.

In preparing milk formulas one can do away with cream and top milk, and by simply diluting and adding sugar a fairly accurate formula can be obtained. If the deficient proteid must be made up, whey can be added to the mixture.

Table 2 has been prepared to enable one to prepare the appropriate formula readily. Fortunately, a little wine cup in universal use among the Chinese measures almost exactly 10 mil. so that this can be used by the most ignorant Chinese woman.

CONCLUSIONS

1. The milk of the water buffalo is a valuable dairy product and contains on an average 12.6 per cent. of fat.
2. This milk can easily be modified for infants' use.

DEXTROSE TOLERANCE IN ATROPHIC INFANTS *

P. M. MATTHILL, K. M. MAYER AND L. W. SAUER

CHICAGO

The tolerance of individuals to sugar has been determined previously by testing how much could be given by mouth or how much could be injected at one time subcutaneously or intravenously before sugar appeared in the urine. It was recognized that these methods were open to objections. In order to overcome these objections Woodyatt¹ constructed an apparatus permitting a continuous intravenous injection of solutions at any desired rate. The apparatus consists of a motor driven syringe filling and discharging automatically. In this way it was possible for Sansum and Wilder² to determine the tolerance of adults to dextrose much more accurately than had been possible before. They found that the appearance of the sugar in the urine depends on the amount of sugar injected in a unit of time, independent of the concentration of the sugar solution. The tolerance is expressed in grams of glucose which can be injected per kilogram of body weight in one hour at a uniform rate of flow, without leading to the excretion of sugar in the urine. For normal adults, dogs and rabbits this tolerance was from 0.8 to 0.9 gm. per kilogram per hour.

We determined the glucose tolerance of atrophic infants by this method with the idea in mind that such infants might derive some benefit from intravenous glucose injections.

The parts of the apparatus which come in contact with the fluid are sterilized by heat. A dextrose marked C. P., manufactured by the Corn Products Refining Company, was used. This is about 99 per cent. pure. The rubber tubing used is 8 mm. in diameter with a 3 mm. bore; a 50 c.c. graduated buret serves as a reservoir. A hand syringe is attached to the two-way stopcock inserted in the tubing between the pump and patient. A glass window connects the tubing with the 22 gage platinum or gold needle. In making the dilution we were guided by the fact that with our instrument the most convenient rate of injection was between 25 and 50 c.c. per hour. The glucose is dissolved in freshly distilled water and arnoldized on three successive days. The strength of the solution was made approximately 10, 15 and 20 per cent. The actual concentration was determined polarimetrically.

* From the Otho S. A. Sprague Memorial Institute Laboratory, Children's Memorial Hospital, Chicago.

1. Woodyatt: *J. Biol. Chem.* **29**:355 (March) 1917.

2. Wilder and Sansum: *Arch. Int. Med.* **19**:311 (Feb.) 1917.

scopically. Buret readings were recorded every five minutes to detect fluctuations in rate. The hypertonic solutions did not cause perceptible changes in the erythrocytes.

The initial rate of injection was chosen just below the tolerance as established for normal adults. A rate of injection must be maintained for thirty minutes to insure a thorough saturation of the tissues before the urine is collected and tested for sugar. As Wilder and Sansum pointed out: "If the rate of injection only slightly exceeds the rate of utilization, glycosuria will occur within this time; if it does not, no glycosuria will occur even after several hours of continuous injection." If no urine is obtained after thirty minutes, the time of injection is lengthened until urine can be obtained. As a rule, the infants voided urine in from one-half to three-fourths of an hour. Catheterization after the beginning of an injection was occasionally resorted to if the infant did not urinate within a reasonable length of time. The urine was tested for sugar with Haines' solution, 1 c.c. of urine being taken for the test. If the urine did not contain sugar by injecting 0.7 gm. per kilogram per hour, the rate was increased to 0.8 gm. per kilogram per hour, and so on, increasing as a rule 0.1 gm. per kilogram per hour until sugar appeared in the urine. In working with the atrophic infants it was soon found to be unnecessary to begin below 1.0 gm. (The urine was always tested for sugar before the experiment was begun.) If sugar appeared in the urine on the first dosage, the experiment was discontinued for the day, as it was not possible to get the urine sugar free within a reasonable length of time. It must be stated, though, that the bladder was not washed out.

If sugar appeared at 1.0 gm. per kilogram per hour the tolerance was taken as 0.9 gm. per kilogram per hour; i. e., 0.1 gm. less than the amount given per kilogram per hour when sugar appeared. The injections were usually started two hours after a feeding, the infants being fed a simple milk dilution with the addition of dextri-maltose.

In the course of our work dextrose solutions were injected intravenously into four nonatrophic infants. These infants ranged in age from 5 to 15 months and were more nearly normal than any of the others. In these cases, the tolerance was found to be 0.8 to 0.9 gm. per kilogram of body weight per hour. These figures correspond very closely to the figures given by Wilder and Sansum for the normal adult. Table 1 gives a summary of these determinations.

The seven atrophic infants studied showed emaciation, tendency to subnormal temperature, lack of turgor and grayish color of the skin. Their weights were stationary or nearly so; the stools were good. In no case was the tolerance below 1.4 or 1.5 gm. per kilogram of

TABLE 1.—RESULTS OF INTRAVENOUS INJECTION OF DEXTROSE SOLUTIONS INTO NONATROPHIC INFANTS

No.	Date	Name	Age in Mos.	Weight in Kg.	Injection Time, Minutes	Gm. per Kg. per Hr.	Sugar in Urine
1	4/19	Tom D.	13½	7.05	30	0.8	0
					30	0.9	0
					30	1.1	÷
2	4/12	Thad. G.	15	9.09	20	0.8	0
	4/16	30	1.0	÷
					30	0.9	—
3	5/16	Sophie	6	4.9	60	0.8	0
	5/23	5.0	30	1.2	—
	5/28	5.0	30	1.0	—
4	5/22	Norma	5	5.4	30	0.9	0
					30	1.0	÷

TABLE 2.—RESULTS OF INTRAVENOUS INJECTION OF DEXTROSE SOLUTION INTO ATROPHIC INFANTS

No.	Date	Name	Age in Mos.	Weight in Kg.	Injection Time, Minutes	Gm. per Kg. per Hr.	Sugar in Urine
1	4/18/19	Francis	5	2.9	30	1.3	0
					30	1.4	0
					60	1.5	÷
2	4/19	Mike L.	6	2.9	120	1.44	0
					30	1.59	÷
	4/24	2.9	90	1.2	0
					30	1.3	0
					15	1.4	0
					30	1.5	0
3	3/15/19	Stephen K.	6	3.18	15	1.63	÷
					30	1.1	0
					30	1.44	0
4	3/31	Charles S.	7	3.46	30	1.66	÷
					30	1.8	÷
5	4/7	Leo L.	..	4.8	60	1.7	0
					30	1.83	÷
	4/8	13	4.77	30	1.43	0
					30	1.67	0
					30	1.63	0
					30	1.75	÷
6	3/24	Viola G.	6	3.2	90	1.7	0
	3/28	3.26	30	1.9	÷
					60	1.8	÷
	4/2	3.46	45	1.6	0
					30	1.8	÷
7	4/30	Marie L.	3½	2.5	30	1.0	0
					30	1.1	0
					60	1.3	0
	5/4	2.87	60	1.6	0
					30	1.8	0
					30	1.9	÷
	5/5	2.87	60	1.6	0
					30	1.8	÷
					30	1.9	÷
	5/7	3.1	30	1.9	÷
					30	1.8	0
					60	1.5	0
					60	1.7	0

body weight per hour (Table 2). Schlossmann,³ Bahrt and Edelstein⁴ and Murlin and Hoobler⁵ found that the metabolism of the atrophic infant proceeded at a higher level than that of the normal infant. Observations of McClure and Sauer⁶ have shown that atrophic infants have a higher surface temperature than normal infants and that there is an increased insensible perspiration. An increased sugar tolerance would seem to fit in very well with such observations.

In Case 7 (Table 2), Marie L., the injections were repeated a number of times for therapeutic reasons. It will be seen that the sugar tolerance in this individual under similar conditions is quite constant. In Cases 2, 5 and 7, and in two cases not included in this report, this same constancy was observed.

SUMMARY

1. The glucose tolerance of the approximately normal infant as determined by the Woodyatt method, is very likely identical with that of the normal adult which is 0.8 to 0.9 gm. per kilogram per hour.

2. The tolerance of atrophic infants for glucose is considerably greater: it varied in our cases from 1.4 or 1.5 gm. to 1.8 gm. per kilogram per hour.

3. Schlossmann: *Ztschr. f. Kinderh.* **5**:227, 1912.

4. Bahrt and Edelstein: *Festschrift, Dr. O. Heubner, Berlin*, 1913.

5. Murlin and Hoobler: *Am. J. Dis. Child.* **9**:81 (Jan.) 1915.

6. McClure and Sauer: *Am. J. Dis. Child.* **10**:425 (Nov.) 1915. McClure and Sauer: *Arch. Int. Med.* **21**:428 (March) 1918.

A CASE OF HYPERSENSITIVENESS TO COW'S MILK *

EDWARDS A. PARK, M.D.

BALTIMORE

When the substitution of a food containing cow's milk for a food not containing it is followed by vomiting and diarrhea, with perhaps other symptoms, it is easy to assume an idiosyncrasy which causes all food containing cow's milk, however intelligently administered, to act like a poison. In all probability, in a considerable number of the cases reported in the literature as examples of hypersensitiveness to cow's milk and a great proportion of those so regarded and treated in practice, the patients suffered merely from ordinary forms of indigestion. Hypersensitiveness to cow's milk has been made the subject of actual proof,¹ like the hypersensitiveness to egg,² to ragweed pollen,³ to pork,⁴ and to other substances through its transference to animals by injection with the patient's blood serum. Strong corroboratory evidence of its existence can be obtained if precipitins are found in the blood,⁵ or by means of skin tests.⁶ Evidence of its existence, essentially the equivalent of proof, may be furnished by clinical data alone, namely,

* From the Pediatric Department of Johns Hopkins University.

1. Schloss, O. M.: Allergy to Common Foods. A Preliminary Report, *Tr. Am. Pediat. Soc.* **27**:60, 1915.

2. Schloss, O. M.: A Case of Allergy to Common Foods, *Am. J. Dis. Child.* **3**:341 (May) 1912.

3. Koessler, K. K.: The Specific Treatment of Hay-Fever (Pollen Disease), in *Forchheimer's Therapeutics of Internal Dis.*, New York and London, D. Appleton & Co., **5**:671, 1914.

4. Bruck, C.: Experimentelle Beiträge zur Aetiologie und Pathogenese der Urticaria, *Arch. f. Dermat. u. Syph.* **96**:241, 1909.

5. The determination of precipitins to cow's milk in the blood of the patient is not sufficient alone to establish proof of a hypersensitiveness to cow's milk, because they have been found in the blood of marantic children who showed no evidence of hypersensitiveness to cow's milk (Moro,⁶ Bauer⁷).

6. Moro, E.: Kuhmilchpräzipitin im Blute eines 4½ Monate alten Atrophikers, München, *med. Wchnschr.* **53**:214, 1906.

7. Bauer, J.: Ueber den Nachweis der präcipitablen Substanz der Kuhmilch im Blute atrophischer Säuglinge, *Berl. klin. Wchnschr.* **93**:711, 1906.

8. Normal persons may give positive skin tests to protein substances to which they give no other evidence of sensitiveness, and conversely persons showing definite evidence of hypersensitiveness to a certain substance may fail to give positive skin tests (Schloss,¹ Longcope,⁹ Blackfan,¹⁰ Cooke and Vander Veer¹¹).

9. Longcope, W. T.: The Susceptibility of Man to Foreign Proteins, *Harvey Lecture*, Philadelphia and London, 1915-1916, p. 271.

10. Blackfan, K. D.: Cutaneous Reaction from Proteins in Eczema, *Am. J. Dis. Child.* **11**:441 (June) 1916.

11. Cooke, R. A., and Vander Veer, A.: Human Sensitization, *J. Immunol.* **1**:201 (June) 1916.

when the ingestion or introduction into the body of quantities of cow's milk altogether too minute to be attended by any consequences in any other condition is regularly followed by characteristic symptoms as in the case now to be described.

CASE REPORT

A. B. C., a boy, was born March 2, 1916, and is now 3 years of age.

Family History.—The aunt on the father's side believes that she has an idiosyncrasy to shellfish, inasmuch as she has twice developed severe urticaria a few hours after eating them. She has eaten shellfish on other occasions, however, without consequences. Both the paternal grandfather and great grandfather were subject all their lives to outbreaks of eczema of unexplained origin. With the exception of these facts the family history on the father's side has no possible bearing on the boy's illness. On the mother's side of the family among the great grandparents, grandparents, and an exceedingly large number of collaterals, no record of any illness which could be interpreted as hypersensitiveness to protein can be obtained. The parents of the patient are both well. Certainly neither has shown any form of protein hypersensitiveness so far as is known. The sister of the patient, $4\frac{1}{2}$ years of age, has never been sick, except for an attack of otitis media, and certainly is not hypersensitive to any of the ordinary foods. No member of the family on either parent's side, for four generations, including collaterals, has been subject to asthma or hay-fever.

The diet to which the mother had always been accustomed was not peculiar in any respect. She had never been in the habit of drinking milk, though she had taken it in tea and coffee, with cereal, and as an ingredient in her food. During her pregnancy she did not alter her usual diet, and during the few days which immediately succeeded the birth of the baby she took milk only in very moderate quantities.

Patient's History.—The birth of the baby was normal; the birth weight was $9\frac{1}{4}$ pounds. The labor lasted twelve hours and was not especially difficult. Physical examination shortly after birth revealed no abnormal condition. The baby was put to the breast on the second day, at six hour intervals, and from the third day on was nursed at four hour intervals. The flow of milk became established on the fourth day. The baby gained from the first at a normal rate. At the end of four months he weighed 17 pounds, and at the end of one year 23 pounds. Except for the illnesses about to be recorded he was never sick; he never vomited, never had loose stools, or showed any variation from the normal. In general his digestion seemed to be extraordinarily good. He had one or two normal stools a day with an almost perfect regularity.

First Two Attacks Following Ingestion of Cow's Milk.—April 13, 1916, when the baby was six weeks old, the 2 p. m. nursing was omitted and a bottle feeding, composed of 1 ounce of cow's milk, boiled for five minutes, 2 ounces of boiled water, and one-half a level teaspoonful of cane sugar was substituted. It cannot be found that the baby had ever received cow's milk previously.¹² Of this artificial feeding the baby refused all but 1 ounce, so that he swallowed altogether not more than 10 c.c. of cow's milk. Unfortunately, he was not carefully observed after the feeding had been given. It is known merely that he went to sleep, remained asleep for some time, and when roused by the nurse vomited. He was excessively pale and "heavy."

12. Although no record that the baby had received cow's milk at the maternity hospital where the mother was confined can be found, such a possibility cannot be excluded.

When offered the 6 p. m. nursing he refused it and vomited again, and then once more fell into a heavy sleep. He took the 10 p. m. nursing, however. By the following morning he seemed much as usual.

Inasmuch as the attack of vomiting just mentioned had occurred without apparent cause, the possibility that the baby might be hypersensitive to cow's milk was considered. Accordingly, one month later (May 11, 1916) when the baby was 10 weeks old, a mixture of one teaspoonful of cow's milk, boiled for five minutes, and one teaspoonful of water was given with the special object of determining whether a quantity of cow's milk too small by any possibility to produce indigestion would cause a recurrence of the illness just described. The baby took only one teaspoonful of the mixture, and therefore swallowed only one-half teaspoonful of cow's milk. Immediately afterward he was put to the breast, which he took in a normal manner. Not very long after the nursing was finished the baby fell asleep. Occasionally he opened his eyes and several times he yawned. His face became flushed. At 5:55 p. m., four hours and fifty-five minutes after he had received the half teaspoonful of cow's milk, he vomited a small amount, and ten minutes later a large amount of bile-stained fluid. He had become exceedingly pale and seemed greatly prostrated. Shortly after the recurrence of the vomiting he had two large loose stools containing mucus. Again he refused the 6 p. m. nursing, and slept heavily until 10 p. m., when he awoke and nursed in a normal manner. The following day he seemed to his mother to be pale and drowsy, but by the third day he was normal.

Skin Reaction to Milk. Attempts at Demonstration of Hypersensitiveness to Cow's Milk by Skin Tests.—May 25, 1916, when the baby was 12 weeks old, an attempt to demonstrate local hypersensitiveness of the skin to cow's milk by means of scratch tests was made. A drop of a 1:10 dilution of cow's milk and one drop each of a 1:100 dilution of goat's milk and of distilled water, the two latter as control substances, were placed at well separated points on the leg and crossed linear scarifications of the skin were made through them by means of clean needles. Traumatic reactions followed immediately at all three points of injury, but a reaction in excess at the site of the scarification through the cow's milk did not develop. Although the cutaneous test with the cow's milk was negative, a delayed general reaction seemed to occur, for the baby fell into the drowsy state previously mentioned, and four hours after the test had been made vomited and had two loose stools.¹³

At about this time a small quantity of goat's milk was fed to the child and produced no symptoms.

13. In the well known case of hypersensitiveness to buckwheat described by Smith¹⁴ a general reaction followed a local skin test. "The left arm was scarified in two places under strict antiseptic precautions. Without the patient's knowledge, an amount containing a grain of buckwheat was taken from a sterilized infusion of the cereal and rubbed into the upper scarification, while a mixture of sterile flour and water was applied to the lower one. The denuded areas were situated about three inches apart. . . . Within fifteen minutes after the vaccination the patient remarked, 'the buckwheat is beginning to work.' He complained of a 'tight feeling' in his chest, and of nausea in the 'pit of his stomach.' He began to cough at frequent intervals, and there was noted increase in the respiratory movements; asthmatic breath sounds; rapid pulse which soon became intermittent; suffusion of the conjunctivae; an erythema, more pronounced on the face, neck, forearms, hands, chest and back than on the buttocks, abdomen and lower extremities; intense pruritus; slight swelling of the features, hands and fingers; giddiness, restlessness and unsteadiness in the gait."

14. Smith, H. L.: Buckwheat Poisoning; with a Report of a Case in Man, Arch. Int. Med. 3:350 (March) 1909.

Intracutaneous Tests with Various Proteins with Resulting Attack.—May 28, 1916, the baby was taken to Johns Hopkins Hospital, and at 1 p. m. was given intracutaneous tests with a series of different protein substances (Table 1) by Dr. K. D. Blackfan. Observations were made by Dr. Blackfan at five minute intervals over a period of half an hour. An area of erythema and edema not exceeding 5 mm. in diameter appeared within the first five minutes at the sites of all the tests, but did not extend sufficiently around any one to make it possible to regard it as positive. At the end of the half hour's observation, at 1:30 p. m., the baby was taken home. During the drive home the baby became much flushed and fell into a heavy sleep. At 3:30 p. m., three and one-half hours after the injections, he awoke, turned white, and vomited twice. He appeared to his mother to be very sick. At 4 p. m., when seen by a physician he was pale, appeared greatly prostrated, and yawned repeatedly. The pulse was 150; respirations 48; rectal temperature 99.2 F. The respiratory murmur was normal. It was then observed that considerable induration, an area measuring roughly 1½ cm. in diameter, existed at the point of injection of the cow's

TABLE 1.—SHOWING RESULTS OF INTRACUTANEOUS TESTS WITH PROTEIN SUBSTANCES *

	Period of Observation					
	5 Min.	10 Min.	15 Min.	20 Min.	25 Min.	30 Min.
Woman's milk undiluted†...	No reaction†	No reaction	No reaction	No reaction	No reaction	No reaction
Cow's milk 1:100 solution....	No reaction	No reaction	No reaction	No reaction	No reaction	No reaction
Egg albumin 1:10 solution....	No reaction	No reaction	No reaction	No reaction	No reaction	No reaction
Beef extract.....	No reaction	No reaction	No reaction	No reaction	No reaction	No reaction
Barley water.....	No reaction	No reaction	No reaction	No reaction	No reaction	No reaction
Horse serum 1:10 solution...	No reaction	No reaction	No reaction	No reaction	No reaction	No reaction
Sterile water.....	No reaction	No reaction	No reaction	No reaction	No reaction	No reaction

* Tests performed by Dr. K. D. Blackfan.

† 0.05 c.c. of each solution injected intracutaneously.

‡ At the point of inoculation of each substance an area of erythema and edema not exceeding 5 mm. in diameter appeared within the first five minutes but, as it did not increase, it was regarded as negative.

§ No observation was made from 1:30 p. m., when Dr. Blackfan made his last observation, until 4 p. m. at the end of the acute attack, when child was seen by doctor. At this time a mass of induration measuring 2.5 cm. in diameter could be palpated about the point of injection of the cow's milk. It was still present the following morning.

milk, whereas none could be found at the points of injection of the other substances. Unfortunately, it is impossible to say at what time the local reaction at the point of injection of the cow's milk developed, because no observation was made between 2 p. m., the hour when the child left the hospital, and 4 p. m., when he was examined by a physician. The induration lasted a considerable time and was still present, though much diminished, the following morning. Following the attack the baby took the 6 p. m. and 10 p. m. feedings in a normal manner, but had two loose stools containing mucus.

Attack Following Feeding of Few Drops of Condensed Milk.—At 10 a. m., June 1, 1916, when the baby was 13 weeks old, he was given through a mistake two to three drops of a solution of one part of condensed milk and twelve parts of water. Within half an hour after he had taken the condensed milk he became drowsy and slept for two hours and fifty minutes. The illness which followed may best be described in the words of the mother. "Waking he vomited violently yellowish green bile, no milk; turned very pale; began to take short panting breaths. His eyes rolled upward. His lips turned blue.

He vomited again and lay exhausted. Turning again deathly white he vomited once more and panted for breath. He was too far gone to cry. His lips again turned blue. He vomited again and had a big green stool." The attack lasted forty-five minutes. The mother thought death imminent. When the physician arrived, more than three-quarters of an hour after the commencement of the attack, the acute symptoms were virtually over. The child was exceedingly pale, and lying motionless on his back on a pillow, with head thrown back and eyes half open, and pupils lost to view beneath the upper lids, giving the impression of being extremely prostrated. The respirations were 46 to the minute but were not especially deep; the pulse was 150; rectal temperature 99.2 F. Examination of the heart, lungs and abdomen revealed no abnormal conditions; the breathing was not asthmatic; the reflexes were normal. Following these alarming symptoms the baby slept for one hour, but took and retained his 6 p. m. nursing. The following day he appeared to be well again except that he was pale and seemed tired.

In the latter part of August a goat was purchased, inasmuch as the supply of breast milk showed signs of failure, and September 30 the weaning from the breast to goat's milk was begun. The weaning, accomplished without difficulty or any event of importance, was complete November 2, when the baby was 8 months old.

Attack Resulting Probably from Ingestion of Bread Containing Cow's Milk.—On the morning of Oct. 31, 1916, when the mother lifted the baby out of the crib she found a large quantity of vomitus on the baby's pillow. Inasmuch as the baby had never vomited on a single occasion, except after the administration of cow's milk, as recorded above, it seemed not improbable that he might have received by accident cow's milk in his food of the previous evening. Although the greatest care was taken at the dairy farm at which the goat was kept, and at the baby's home where cow's milk was used for the other members of the family to prevent the entrance of cow's milk into his food, accidents of this nature could not be precluded absolutely. On telephoning to the dairy and on questioning the servants in regard to the preparation of the baby's food on the previous day, no evidence that the baby had received cow's milk could be found. A clue was finally supplied, however, by the cook, when she said that at 6 p. m. she had seen the baby eat a piece of baker's bread about as large "as the end of the thumb" given to him by his sister. On communicating with the bakery the information was obtained that milk had been used in the preparation of the bread. A week later the baby was given a piece of bread of a corresponding size made without milk, but manifested no symptoms.

Renewed Attempts at Demonstration of Hypersensitiveness of Cow's Milk.—Some time in the latter part of December (the exact date not recorded) another attempt to demonstrate hypersensitiveness to cow's milk by means of a skin test was made. The technic employed was this time that advised by Craig for the cutaneous test with tuberculin. A drop of cow's milk and of goat's milk were placed on the skin of the leg at the same distance from each other, and six or more punctures of the superficial portions of the skin made through them. The tests were started at 1:15 p. m. At 1:25 p. m. a wheal about 3 mm. in diameter had developed about each point of scarification surrounded by a faintly pink areola. The two test areas were observed for more than two hours, and though the inflammatory reaction around the test made through the cow's milk became slightly larger than that made through the goat's milk no well marked difference developed. Jan. 7, 1917, these tests with the cow's milk and goat's milk were repeated. Ten minutes after the tests had been made a tiny wheal surrounded by a faintly pink areola appeared about the scarification through the goat's milk, whereas an oval area of redness about 3 cm. long and 1.5 cm. wide, with considerable central induration, developed

at the site of the test made through the cow's milk. Three quarters of an hour after the tests had been made the red areola about the point of inoculation with the cow's milk had decreased slightly, but could be seen across the room, and could easily be palpated, whereas the reaction about the site of the goat's milk test remained essentially as before. No constitutional reaction of any sort was observed after these two cutaneous tests.

Desensitization to Cow's Milk.—Sept. 10, 1917, when the baby was 18 months of age, it was determined to make an attempt to desensitize him by the administration by mouth of minute quantities of cow's milk. Accordingly, at 8 a. m. with the morning feeding 0.001 c.c. of cow's milk was given. The baby showed no symptoms until the afternoon, when he became pale and appeared sick, lying down, refusing part of his food, and crying as if in pain. Becoming worse in the evening the temperature was taken and found to be 102 F. Examination revealed otitis media, fully explaining the baby's condition. Further attempts at desensitization were, therefore, deferred. The baby recovered from the otitis media in about two weeks, but remained pale, and appeared to lack his former vigor for several weeks afterward.

Nov. 4, 1917, the attempts at desensitization were renewed. The baby was now 20 months of age. He had begun to stand at the age of 12 months, and to crawl vigorously at 15 months, but had not walked alone until 18 months. As soon as he was able to crawl from one part of the house to another, and particularly after he had learned to walk, it had become increasingly difficult to safeguard him against the ingestion of food containing cow's milk. On a number of occasions he had succeeded in obtaining crumbs of baker's bread and more than once bits of buttered toast which had fallen on the dining room floor or had been given to him by his sister, who seemed bent on bringing about his discomfort whenever possible. In spite of the fact that the particles of food which he succeeded in eating often must have contained traces of cow's milk he had not once become sick. It seemed probable, therefore, that he had partially at least desensitized himself, or had begun to outgrow his hypersensitiveness. Accordingly, it was determined to administer one drop of undiluted cow's milk as an initial dose. Nov. 4, 1917, this was done; at 8:40 a. m. one drop of cow's milk was given followed immediately by breakfast. After the ingestion of the one drop of cow's milk no effect was noted. There was no drowsiness or vomiting and the pulse remained unaltered. November 5, two drops were given at 8:20 a. m. with the breakfast without the production of any change in the baby's condition. On November 6, at 8:20 a. m., four drops were administered with the breakfast. At 9:30 a. m., the baby, who had been playing about the dining room table, suddenly stopped, turned pale, and lay down on the floor on his side with his head on the rug, which he had never done previously. He was immediately taken up and put to bed, where he slept for some time. He did not vomit. The rectal temperature was 99.2 F. November 7 he was given five drops of cow's milk at 8 a. m. At 9:15 a. m. he again became pale, stopped his play, and lay down on the dining room floor. He was again placed in his crib, but at the end of an hour seemed to have recovered entirely. His temperature remained normal and no vomiting occurred. November 8 he was given ten drops of cow's milk with his breakfast at 8:15 a. m. At 9:15 a. m. it was noticed that he had turned pale, and at 9:30 a. m. he went to sleep for half an hour. Ordinarily he never became sleepy at this time. November 9 he was given fifteen drops with his breakfast at 8:15 a. m. At 9:15 a. m. he appeared paler than previously, but did not become drowsy. November 10 he was given thirty drops at 8 a. m., and November 11, sixty drops, but showed no symptoms. November 12 he received 7.5 c.c. of cow's milk at 8:15 a. m. At 9:50 a. m. he appeared pale, went to his nurse, lay on her lap for ten minutes very quietly, then climbed down again and began

to play in a normal manner. November 13 he received 10 c.c. without the production of any symptoms. From November 13 on he showed no symptoms after the ingestion of quantities of cow's milk, which were steadily increased, first by 1 c.c. daily (November 16 he received 14 c.c.), then by 2 c.c. (November 17 he received 16 c.c.), and finally by the addition of 3 c.c. (December 1 he received 60 c.c.). December 2 he was given a cup of cow's milk instead of goat's milk, and by December 10 he took one-half liter, the goat's milk being omitted altogether.

Present Condition.—Now, at 3 years of age, the child is perfectly well. He drinks regularly a pint of cow's milk daily. He does not dislike his milk, but does not care for it especially, always drinking water in preference to it, and regularly leaving it until the last. He has had another attack of otitis media, and a few days ago on coming from Florida to his home in Baltimore he broke out with an eczematous eruption which could not be explained. He has had no recurrence of symptoms such as have been described. It is certain that the child is not affected by egg.

Perhaps the most unusual feature of the case was the delay in the development of the anaphylactic response, which in the early period did not reach its climax (as indicated by the act of vomiting) for from three to more than four and one-half hours after the ingestion of the cow's milk, and not for three and one-half hours after its introduction under the skin. It does not seem probable that the delay was caused by slow passage through the gastro-intestinal tract or slow absorption, because the same delay occurred after the injection of the milk into the skin. The data at hand are too limited, however, to permit speculation.

Another interesting feature of the case is that the sensitiveness, though apparently exceedingly marked in the earlier months of life, exhibited a tendency to disappear spontaneously rather early. As already pointed out, however, the child may have succeeded in desensitizing himself to a certain extent when he became old enough to crawl about and find crumbs of food sometimes undoubtedly containing traces of cow's milk. The interval between the time of ingestion of the milk and the full development of the symptoms also seemed to diminish as the child became older (Table 2). When desensitization was begun at the age of 20 months, it will be remembered, the symptoms appeared within an hour and one quarter if at all. It was impossible to determine exactly at what moment the reaction began, and, therefore, the true incubation interval could not be measured. As has happened in the experience of others, the cutaneous tests failed to give clear indication of the actual condition. The single intradermal test did, however, give an unequivocal reaction which was late in development like the symptoms. It indicated that the subcutaneous tissues or blood possessed the capacity to react in the presence of a sufficient concentration of antigen. Only in one of the attacks were symptoms present which indicated that the reaction had extended beyond the gastro-

intestinal tract and involved other parts of the body, namely, the attack of June 1 which followed the ingestion of three drops of condensed milk. On that occasion, it will be recalled, severe respiratory symptoms were present. On all other occasions the clinical manifestations were limited to drowsiness, flushing of the face, yawning, later pallor, vomiting, prostration, anorexia and diarrhea. Though the reaction may have been systemic, there was never any clinical indication that such must be the case, with the exception, perhaps, of the attack of June 1 to which reference has just been made.

TABLE 2.—IMPORTANT DATA IN REGARD TO REACTIONS OF PATIENT TO COW'S MILK

Date	Age	Quantity of Milk	Mode of Administration	Interval between Entrance of Milk into Body and Full Development of Symptoms	Symptoms
4/13/16	6 wks.	$\frac{1}{2}$ oz.	Mouth	$3\frac{1}{2}$ to 4 hrs.	Pallor, drowsiness, vomiting
5/11/16	10 wks.	$\frac{1}{2}$ teaspoon-full	Mouth	4 hrs. 55 min.	Drowsiness, flushed face, yawning, vomiting, prostration, diarrhea
5/25/16	12 wks.	One drop of a 1:100 solution	Skin (scarification)	4 hrs.	Drowsiness, vomiting, diarrhea
5/28/16	12½ wks.	0.01 c.c.	Skin (intra-dermal injec.)	$3\frac{1}{2}$ hrs.	Local induration of skin at site of test; drowsiness, flushing of face, later pallor, vomiting, yawning, prostration, diarrhea
6/ 1/16	13 wks.	2 to 3 drops sweetened condensed milk	Mouth	2 hrs. 50 min.	Drowsiness, repeated vomiting, pallor, dyspnea, cyanosis of lips, great prostration, diarrhea
11/ 6/17	20 mos.	4 drops	Mouth	1 hr. 10 min.	Pallor, drowsiness, faintness, no vomiting
11/ 7/17	20 mos.	5 drops	Mouth	1 hr. 15 min.	Pallor, drowsiness, faintness, no vomiting
11/12/17	20 mos.	7.5 c.c.	Mouth	1 hr. 35 min.	Pallor, drowsiness, faintness

There was never any depression of the temperature. Moreover, the child, so far as is known, never passed into an anti-anaphylactic state. The reaction of May 11 did not prevent the reaction of May 25 from taking place, and the severe reaction of May 28 did not prevent the still more severe reaction of June 1 from occurring. It seems necessary to assume either that the provocative dose of cow's milk was insufficient to produce a systematic reaction of sufficient magnitude to confer temporary immunity, or else that the reaction was essentially a local one, limited to the gastro-intestinal tract. Again, however, speculation is not justified.

The existence of hypersensitiveness to cow's milk in an infant of six weeks who had never been known to receive cow's milk previously makes it necessary to regard the condition as prenatal in origin. The possibility that the hypersensitiveness was derived passively from the mother is excluded, if for no other reason, by its duration. In the absence of evidence that the peculiarity was acquired it must be regarded as having been inherent in the germ plasm.

The writer wishes to express his thanks to Professor Howland and to Dr. K. D. Blackfan and Dr. G. Powers for their advice and assistance.

CLINICAL DEPARTMENT

A CASE OF ANOMALY OF THE DIAPHRAGM

WITH HERNIATION INTO THE THORAX OF CERTAIN VISCERA RESULTING
IN A GASTRIC AND INTESTINAL OBSTRUCTION

L. R. DEBUYS, B.S., M.D.

Professor of Pediatrics, School of Medicine, Tulane University

NEW ORLEANS

REPORT OF CASE

Dorothy C. was admitted into my service at the Touro Infirmary May 2, 1919. She had been ill two days prior to admission and was sent to the institution by a physician with the diagnosis of "locked bowels."

Past History.—She was four months and five days old, and was the only child of apparently healthy parents. There was no history of miscarriage and the delivery of the patient was normal, except that the cord was wound around the neck. No instruments had been used. She had had no "blue" spells, and had been perfectly well and healthy up to the age of three months when she had a peculiar attack of colic with twisting and straining. This "spell" was promptly relieved by the administration of milk of magnesia and an enema, after which she "got all right." Another similar attack occurred between the first one and the one for which she was admitted. It was a little more pronounced than the first, but she promptly recovered from it also, the same treatment being employed.

Present Illness.—Two days previous to admission her parents had gone on a trip to the lake shore, and while there the patient began making a grunting noise. On the way home a "weak spell" occurred, and on reaching home the baby wanted to vomit, but could not. From this time on she could not nurse. What was taken would come up immediately as it went down. Her bowels, however, moved this day. The next day the grunting continued, becoming worse as time passed. Attempts were made as on the two previous occasions to overcome the condition, but it was impossible to give anything by mouth as she would "not swallow it," and enemas brought back nothing. She became progressively worse and was in a desperate condition when I saw her for the first time.

Physical Examination.—Dorothy was an apparently well developed and well nourished baby, acutely ill, with a rapid respiration, 78 per minute, and a pulse of from 150 to 160 per minute. Her temperature was 103 F. and rapidly rose to 104 F. The respirations were suggestive of a pneumonia, being jerky, and with a respiratory grunt, accompanied with movements of the alae nasi. On inspection, the chest showed less movement on the left side both anteriorly and posteriorly, and it was apparently not as full as on the right side. Palpation revealed less fremitus on the left side as compared with the right side. On percussion the resiliency of the right thorax seemed normal, but it was absent on the left side, and the notes elicited were different. On the right side the note was apparently normal or probably a little hyperresonant, while on the left side it reminded one of a note with an element of tympany. On auscultation, the voice and respiratory sounds on the right side were distinctly puerile, while on the left side they were absent. There were no râles. The heart was displaced to the right, the apex beat was in the median line on its normal level.

* Read before the American Pediatric Society, June, 1919.

The abdomen was flat and soft, and presented a tumor in the epigastric and left hypochondriac region. It was lying transversely, was about the roundness of a small banana, and seemed to be from three to four inches long. It was distinct from the lower border of the ribs. It was immovable. The liver was normal; the spleen could not be differentiated from the tumor. Otherwise the abdominal examination, as well as the rest of the physical examination, was negative.

A digital examination was made which showed no tumor in the pelvis nor in either of the regions of the descending or ascending colon, but there was a tumor conforming to the one already described, slightly boggy, and in places giving the sensation of fluctuation.

Blood Examination.—The blood examination showed a total leukocyte count of 29,500 with an 88 per cent. polymorphonuclear-neutrophilic cell count.

A bismuth enema was given with the baby in an inclined plane of about 30 degrees, head down. Only a small quantity of the enema could be given, as the baby would expel it promptly and at regular intervals, so that the time was judged and just before the enema was expelled a roentgenogram was made (Fig. 1). This clearly showed an obstruction. The roentgenogram suggested an intussusception. Remembering, however, the physical findings of the chest with the displacement of the heart to the right, the thorax in the picture was read. This showed a decided shadow on the entire left side. As the shadow was on the side where the physical findings were decidedly against even the suggestion of a pneumonia, and as the duration of the illness was hardly sufficient to have produced an empyema, and as an empyema sufficient to produce a displacement of the heart would at least not have given to the thorax an appearance of being not as full as the opposite side, the surgeon, Dr. Russel E. Stone, who was called in for operation for the obstruction, was requested to look for the possibility of a diaphragmatic hernia. This was shown to exist at the operation.

Operation.—Assisted by Drs. J. M. Gage and J. D. Rives, and with the patient under ether anesthesia administered by Dr. A. B. Pitkin, Dr. Stone performed the operation which he describes with his findings as follows:

"An incision was made in the midline extending from the umbilicus to about an inch above the symphysis pubis. The peritoneum was opened showing the usual amount of clear, straw-colored fluid in the abdomen. The intestines were found empty and contracted, and of normal color; the peritoneum was glistening and not congested; no omentum was visible. Palpation under the upper angle of the incision revealed a tense fluid tumor under the left costal arch, about the size of an ordinary goose egg; inspection showed this tumor to be of the color of gangrenous bowel with blood vessels standing clearly on the surface; some hemorrhagic areas were also visible. On palpating the tumor there was a sudden gush of a blood tinged watery fluid through the nostrils and mouth; at this point there was a cessation of breathing, and all attempts at resuscitation were futile. The incision was then prolonged upward to the left of the umbilicus, almost to the xiphoid; the great omentum and transverse colon were still not visible. The spleen was now seen lying on top of the tumor, with its long axis transverse to the abdomen and its convex surface lying against the diaphragm, and the lower edge just under the left costal arch. It was intimately adherent to the tumor on its anterior aspect.

"A complete exploration of the upper abdomen was now made; the liver and gallbladder were found to be normal, but the tumor was attached to the hilum of the liver; the transverse colon was still not in sight. Digital examination revealed a hiatus in the diaphragm under the tumor which was distinctly felt to be continuous with another fluid mass in the thorax. The incision was now prolonged upward to the left of the sternum, the costal car-



Fig. 1.—The shadow in the left side of the chest is quite apparent, and inasmuch as the heart was displaced to the right, a diaphragmatic hernia was suspected.

tillages were divided, and the left chest opened revealing the fundus and the greater part of the body of the stomach, the transverse colon and great omentum in the thoracic cavity. No pleural sac was found over these viscera, they were of normal color; the stomach was distended and the colon empty. (Fig. 2.)

"The diaphragm was divided down to the hiatus. The tumor consisted of the pyloric portion of the stomach twisted on its axis at the hiatus behind the diaphragm, so that the greater curvature with the attachment of the gastro-splenic omentum lay in contact with the inferior surface of the diaphragm, under the left costal arch. Thus the pyloric portion of the stomach was

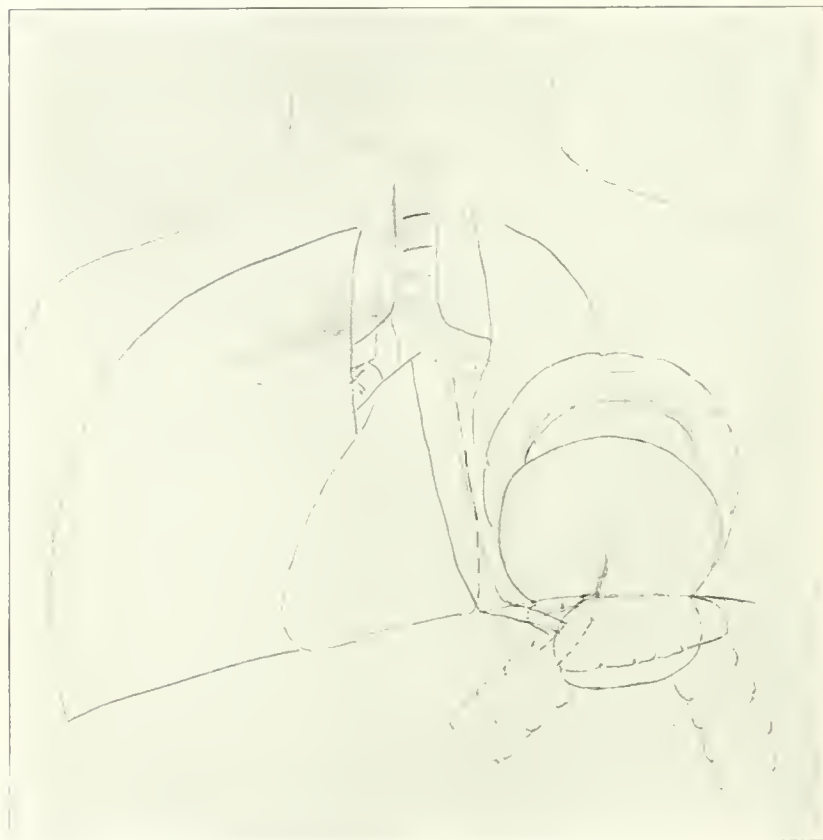


Fig. 2.—Schematic relations of viscera in thorax and in abdomen.

strangulated and the pylorus closed by torsion, while the portion of the stomach in the chest cavity was not strangulated. The transverse colon and omentum had slipped up behind the stomach.

"The left lung was collapsed and showed no evidence of pneumonia. The heart was displaced to the right so that the apex lay on the spinal column at about the fourth chondrosternal junction. The wound was closed with two layers of continuous catgut sutures."

Diagnosis.—Diaphragmatic hernia containing the stomach, transverse colon and great omentum.

Being desirous of more information with regard to the diaphragm and left thorax and the displacement of the heart, after much persuasion a partial necropsy was granted by the parents under the agreement that the body, the abdomen and thorax only, were to be inspected without removal of any tissue, and that the necropsy was to be done through the wound resulting from the operation. The necropsy was performed by Dr. C. W. Duval, whose report is as follows:

NECROPSY REPORT

The body was that of a baby well developed and well nourished, about four months of age. The interior of the abdomen and thorax were exposed by opening the wound resulting from the operation, which extended from slightly below the umbilicus upward to the right of the xiphoid process; the intercostal cartilages of the lower ribs had been incised. A good view of the abdomen and thorax was obtained. On inspection, the lower end of the esophagus and the first portion of the duodenum were found to be ligated and the stomach and spleen missing; the latter had been removed at the time of the operation after the death of the child. The left suprarenal was found to be enlarged and hemorrhagic, and was removed for microscopic study. The small and large intestines were normal.

The diaphragm was next examined very carefully; the normal openings (vena caval, esophageal and aortic) were intact and presented no defects; its attachments were normal, except in its posterior left half. From a point 6.5 cm. from the vertebral column, for a distance of 5 cm. at the level of the sixth rib (at which point it became attached again), there was no attachment; there was a hard cord bridging over this area in a dome-like manner. This section of the diaphragm was removed.

The left lung was found to be atelectatic, except for a small portion of its periphery. The heart was displaced to the right side; the apex was beneath the sternum. The right lung was found to be perfectly normal and had been functioning properly.

The stomach appeared bent on itself at a point from above downward beginning at the esophageal end anteriorly. There was another twist that appeared to be anterior to the pyloric orifice. The twisting in these two portions had cut off certain blood supplies which resulted in gangrenous necrosis of the stomach wall. There were three different areas of gangrenous necrosis. One was on the anterior surface of the stomach beginning along the lesser curvature at the pylorus and extending to the esophageal orifice; this area extended down over the anterior surface of the stomach in a fanlike manner for a distance of 5 cm. The second area of gangrenous necrosis appeared posteriorly and was about the size of a 50-cent piece; its situation was near the lesser curvature. The third gangrenous area, the longest of the three, included almost all of the fundus for the anterior surface of the stomach.

The transverse mesocolon and the gastrosplenic omentum also showed definite areas of gangrene. The stomach contained much coagulated and liquid blood.

The spleen, aside from marked congestion, appeared normal.

The section of the diaphragm removed for study showed the band to consist of a crude cordlike mass, thicker in the center than at its attachment ends. The cross section measurement at the center was 4 mm. and at the ends 2 mm. This cordlike bridge was perfectly smooth and glistening in its entire extent.

Microscopically, the cross section of the cord showed a central mass made up of aggregated bundles of muscle fibers for the most part running in one plane along the length of the cord. There were, however, those bundles that were in other planes running more or less oblique to the long diameter of the cord. This central core of muscle bundles was enveloped for 90 degrees of the arc by a normal zone of connective tissue; over this zone of connective tissue there was attached the pleural and peritoneal serous membranes.

Throughout the pancreas there was extensive necrosis both of the acini and the Langerhans islands, except in a few small areas at the tail, which were in a normal state of preservation. The necrosis of the pancreas had undoubtedly resulted from a twisting of the organ in such a way as to hurt its blood supply. The absence of fat necrosis in the abdominal tissues at necropsy further indicated that the destruction of the pancreas was quite recent.



Fig. 3.—Diaphragm seen from below upward. Error of attachment on left side.

The left suprarenal showed also that its blood supply had been interfered with because of the extensive hemorrhage that appeared in the medulla. The cortical tissue appeared not affected. The right suprarenal was negative.

DISCUSSION

This case showed many points of interest. The two previous attacks were probably caused by a slight involvement of the intestine through the abnormal opening, but the fatal attack apparently began with an involvement of the stomach and later because of the straining the colon became complicated. In substantiation of this fact may be

offered the gangrene of the stomach and the normal tissues of the intestine found at operation. Again the bowels discontinued moving the day following the onset of the attack showing the colon to be free later than the stomach; also there was no distention of the intestines either small or large, due to the fact of their having become relatively emptied after entrance of food from above and exit of the food from below before obstruction of the colon.

The obstruction of the stomach is of extreme interest both because of the pressure with occlusion at the cardia and the twisting of the pylorus with its obstruction at the point of entry into the thorax. The fatal termination was probably due to shock. The blood-tinged watery fluid which came through the nostrils and mouth was part of the contents of the stomach expelled when the pressure at the cardia was relieved. While the baby died of shock at the time of operation it is hardly probable that the outcome of the case could have been different because of the physical condition of the patient, the duration of the obstruction, and the gangrenous condition of the stomach.

The absence of tenesmus with bloody stools in an obstruction involving the descending colon should require the exclusion of the diagnosis of intussusception. The roentgenogram without any evidence of air in the thorax, especially with an intestinal herniation into it and without any shadow due to bismuth, is of decided interest (Fig. 1).

This hernia belongs to the false variety of the congenital type of diaphragmatic hernia being differentiated from the true variety by not having a sac. In this instance there existed two conditions not mentioned in the various classifications of diaphragmatic hernias, namely, strangulation and palpable abdominal tumor.

The defect of the diaphragm (Fig. 3) in this case was a developmental error which occurred at the point at which in the developmental progress of the membranum transversum the attachment is completed last, namely, on the left side and posterior aspect.

PROGRESS IN PEDIATRICS

RÉSUMÉ ON THE CIRCULATORY SYSTEM

REVIEW OF LITERATURE OF 1917, 1918 AND 1919

HENRIETTA CALHOUN, M.D.

IOWA CITY, IOWA

THE HEART AND AORTA

The study of the *normal heart action* is attracting an increasing amount of interest. Keith¹ calls attention to the fact that the heart functionally consists of a central pump, the left ventricle, with three subsidiary loading pumps, the right and left auricles, and the right ventricle. Each chamber has a fulcrum, that of the auricle being applied through the fixation to the dorsal pericardial walls and through the pericardial extensions on the pulmonary vessels and lungs to the costal and diaphragmatic chest wall; the ventricles have two fulcrums, the fixed ascending stem of the aorta, and the movable fulcrum at the apex.

With ventricular contraction the auricular base about the mitral and the tricuspid rings is reduced in size and through the action of muscles acting from the apical fulcrum is drawn down toward the apex, enlarging the auricles. This is the key to the venous pulse. The aortic base is unchanged and becomes the fulcrum from which the expelling musculature works. The muscles of the heart are arranged in groups of antagonistic muscles. In the left ventricle there is a circular expelling coat set between an outer and an inner spiral coat, the fixed axis passing from the mouth of the aorta to the apex. In systole the muscles approach this axis. All of the muscular coats ultimately end in the fibers of the internal spiral coat of the left ventricle, each segment narrowing or expanding on the principle of the iris diaphragm. The auriculoventricular bundle ends in the trabecular network of the apex where ventricular systole begins. The antagonist muscles are the internal muscles of the columnae carnae and the papillary muscles which extend from the apex to the base of the auricles and the aorta, and the external spiral muscles on the outside of the ventricle wall which end at the aortic and auricular bases. These groups are antagonistic to lengthening of the heart chamber. In early systole when the auricular base descends, the circular fibers are more than antagon-

1. Keith, Arthur: Brit. M. J. 1:361 (March 30) 1918.

ized, but in the later phase of systole the circular fibers become dominant, and raise the auricular base. The apico-aortic fibers are sustaining and do not change in length during systole.

In the right ventricle, the pulmonary orifice is not fixed, the infundibular bands from the right base acting as the fulcrum. The septum really belongs to the left ventricle and is only passively a wall of the right, so that the internal musculature running from the apex to the base is more highly developed on the right, with the pectinate muscles forming an opponent set.

Smith² has an interesting study of the anatomy of the coronary arteries obtained by injecting the arteries with physiologic sodium chlorid solutions until the fluid returns clear and then injecting a solution consisting of 2 parts of barium suspended in 10 parts of water with a little tragacanth. Stereoscopic roentgenograms are made, and he finds studying thirty dog hearts and twenty human hearts that the coronary arterial distribution is very analogous in the dog and man. The youngest heart studied is that of a 6 months old infant.

Minerbi³ studied the *responses of muscular tone* in the heart chamber. A series of twenty strokes with the percussion hammer, is followed by retraction of the antrum, auricle or ventricle according to the line of strokes, of from 1 to 2 or more cm. inside of the previous outline. The normal retraction often totals 4 cm. for the heart in three minutes. Auricle, antrum and ventricle can retract independently of each other. In a normal heart, with the patient horizontal, if an attendant passively raises the legs to an angle of 75 or 80 degrees, then allows the patient to lower them slowly, there is definite retraction of the auricles, while with myocardial weakness the auricles or both auricles and ventricles dilate.

The *electrocardiograph* may be used to differentiate benign lesions in cardiac children from the serious cases with a bad prognosis. Halsey⁴ says the most distinctive feature of *heart muscle function* is rhythmic contraction. The rate of conduction of the impulse in the ventricle is about 400 mm. per second, in the auricle about 1,000 mm. per second and in the Purkinje network the conduction rate is five times that of the other ventricular fibers. The left auricle contracts 0.013 second later than the right auricle, and the ventricular contraction is 0.2 second later. This interval between auricles and ventricles is the *P-R* time. Each contraction calls forth the full power of the heart muscle cells, and is followed by a period of rest. At the onset

2. Smith, F. M.: Am. J. M. Sc. **156**:706 (Nov.) 1918.

3. Minerbi, C.: Revista Crit. di Clin. Med. **18**:213 (May 12) 1917; abstr. J. A. M. A. **68**:2011 (June 30) 1917.

4. Halsey, R. H.: Arch. Pediat. **34**:128, 1917.

of systole there is a short refractory period during which outside stimuli have no effect. The contraction wave passes from the right auricle to the left auricle, through the auricular-ventricular bundle to the ventricles. The *R* wave on the graph is the ventricular contraction or the apex beat and the radial pulse. At 72 beats per second the interval between *R* waves is 0.6 second. Halsey took records on ninety-two children. Irregularities due to auricular and sinus variations in time are benign, while disturbances of the ventricular rate and rhythm, dissociation of ventricle from auricle, and auricular fibrillation are of serious import. The vital importance of differentiating between benign and serious cases of cardiac disease in children is seen when, according to Holt,⁵ there are 25,000 cardiac children in the New York public schools; while Ferguson⁶ places the figure somewhat higher, one in every fifteen children. Wilcox⁷ points out that 49 per cent. of the children seriously incapacitated by cardiac conditions may be discharged from care in a country sanitarium able to lead a normal life.

Brown,⁸ reporting the tenth case of *paroxysmal tachycardia in children*, says that vagal influences or local lesions may depress the normal point of origin so that the pacemaker rôle may be assumed by other parts. Lesions in the endocardium or myocardium may cause abnormal rhythm. In auricular fibrillation and paroxysmal tachycardia the excitation waves are of ectopic origin arising below the sino-auricular-node. The auricle responds to each stimulus. In auricular flutter the rate is from 240 to 360 per minute, causing a fatigue block in the bundle of His so that only a small portion of the impulses pass to the ventricle. In children the auricular rate of paroxysmal tachycardia is seldom more than 200 to 250 per minute.

In auricular flutter and auricular fibrillation Cohn and Lundsgaard⁹ call attention to the fact that with irregular and uniform beats of the heart, the systolic and diastolic *pulse pressure* varies, especially in the large arteries. At the junction of the small arteries and capillaries there is a point where the head of pressure becomes effective. Using Gaertner's method of blanching the finger by rolling a thick rubber ring down from the apex, a small pneumatic cuff is applied to the basal phalanx. This is connected with a pump and a manometer and the pressure raised, then the rubber ring is removed and as the pressure falls gradually in the manometer system, the point where color returns

5. Holt, L. E.: Arch. Pediat. **34**:12, 1917.

6. Ferguson, J. S.: Arch. Pediat. **34**:269, 1917.

7. Wilcox, H. B.: Arch. Pediat. **34**:43, 1917.

8. Brown, N. W.: Am. J. Dis. Child. **14**:287, 1917.

9. Cohn, A. E., and Lundsgaard, C.: J. Exper. M. **27**:505 (April) 1918.

to the finger marks the point where the manometer pressure equals the blood pressure. This reading in eight normal individuals averaged 20 below the brachial pulse pressure.

Bass¹⁰ considers *heart block* as an abnormal heart mechanism in which there is delay in, or absence of the response of the ventricle to the auricular impulses. The time of passage of the cardiac impulse as shown by the electrocardiograph varies with the age; in infancy being 0.10 second; in childhood 0.13 second, and at puberty 0.14 second. The distance on the electrocardiogram between the *P* wave (auricular systole) and the *Q R S* group (ventricular systole) is lengthened in heart block, with an increase in the *a-c* interval in the phlebogram. He reports heart block associated with a congenital heart lesion in a boy 15 years old. This is the fifth case in the literature of heart block due to congenital malformation. Septal defects do not involve the auriculo-ventricular bundle. Most cases of heart block in children are due to acute inflammatory conditions. Parkinson¹¹ reports heart block in a child after an acute attack of pneumonia during which the temperature rose to 109.6 F.

Brown¹² presents a case of sino-antral block in a child 11 years of age, in which the arrhythmia was eliminated by atropin without causing any acceleration of the heart rate. Cockayne¹³ from the Royal Naval Hospital reports on heart block and bradycardia following influenza, in seventy-one patients, 20 years old and under; 2:1 heart block occurred in eight cases; 3:1 heart block occurred in four cases and simple bradycardia in fifty-nine cases.

In studying the functional capacity of the right heart Calandre¹⁴ notes that the first sign of *myocardial weakness* is the loss of muscular tone during the rest period. In the right heart this modifies the venous pulse. The normal venous pulse has three waves, *a*, *c* and *v*; to these with a slow heart beat is added a fourth wave, the *s* or *h* wave occurring during diastole following the *v* and preceding the *a* wave. With atony of the right myocardium this fourth wave is absent during those periods when inspiration coincides with the resting phase of the heart.

To locate the *electrical axis of the heart*, Carter, Richter and Green¹⁵ make use of an equilateral triangle inscribed within a circle

10. Bass, M. H.: J. A. M. A. **70**:287 (Feb. 2) 1918.

11. Parkinson, J. P.: Lancet **1**:184 (Feb. 3) 1917; Brit. J. Child. Dis. **14**: 112, 1917.

12. Brown, N. W.: Arch. Int. Med., **21**:458 (Oct.) 1919.

13. Cockayne, E. A.: Quart. J. Med. **12**:409 (July) 1919.

14. Calandre, L.: Arch. d. Mal. du coeur. **10**:651 (Dec.) 1917; abstr. J. A. M. A. **70**:574 (Feb. 23) 1919.

15. Carter, E. P., Richter, C. P., and Green, C. H.: Bull. Johns Hopkins Hosp., **30**:162 (June) 1919.

divided into degrees, the horizontal axis corresponding to the 0—180 degree line. Each side of the triangle represents a lead, the side parallel to the horizontal axis representing Lead I. Coordinate squares are drawn within the triangle corresponding to each side. Then from the electrocardiogram reading of R and S — counting down from the side representing Lead I to the point where it intersects the reading of R_3 and S_3 of Lead III — one gets a point through which the radius showing the direction of the electrical axis passes. This is important because the manifest value or maximal distance separating two points between which there is developed potential difference is met only when the electrical axis and the lead employed lie in parallel planes.

After the heart has stopped beating, and the index of muscular contraction has ceased to record, the electrocardiogram continues to register. Einthoven and Hugenholtz¹⁶ demonstrate that the apparatus used for *measuring the index of muscular contraction* is not sensitive to the slighter movements of the heart, and so does not register the exact instance when contractions cease.

Morison¹⁷ uses inhalation of *amyl nitrite* to increase the flow of blood through the auriculoventricular ring, thus favoring the production of the murmur of mitral stenosis. In six out of twelve uncertain cases of mitral stenosis an unmistakable presystolic murmur was demonstrated.

Smith¹⁸ calls attention to a double *click-like sound* corresponding in time to the heart sounds, which is either faint or like the click of the telephone receiver, that occurs *in wounds of the chest*. He believes it is due to interstitial emphysema in the connective tissue of the lungs or mediastinum.

Heart massage was successfully employed by Mollison¹⁹ in a case of heart failure under chloroform and ether anesthesia during an operation for the removal of adenoids and tonsils. An abdominal incision was made and thirteen minutes after the heart stopped massage was begun, and kept up for four minutes, when the heart began to beat. Fisher²⁰ used heart massage without operation on an infant born in pallid asphyxia. He pressed the right fingers deeply into the right epigastrium bringing them under the ribs and against the heart by invaginating the abdominal wall, then with the left fingers pressed on the chest at the left nipple, five or six quick thrusts started the heart to

16. Einthoven, W., and Hugenholtz, F. W. N.: *Nederl. Tijdschr. v. Geneesk.* **1**:310 (Jan. 25) 1919; abstr. *J. A. M. A.* **72**:1114 (April 12) 1919.

17. Morison, R. A.: *Brit. M. J.* **1**:452 (April 20) 1918.

18. Smith, S. M.: *Brit. M. J.* **1**:78 (Jan. 19) 1918.

19. Mollison, W. M.: *Brit. J. Child. Dis.* **14**:42, 1917.

20. Fisher, F. C.: *Brit. M. J.* **2**:215 (Aug. 18) 1917.

beating, and with artificial respiration breathing was begun in five minutes. Bost and Neve²¹ make a median abdominal incision above the umbilicus, then from the inside they cut the fibers of insertion of the diaphragm under the left costal margin, and introducing the right hand through the stretched opening into the thorax, the heart within the pericardial sac is grasped, with the right thumb resting under the sternum, and the fingers resting on the posterolateral surface of the pericardial sac, massage is applied.

Poynton²² emphasizes the *effect of rheumatic infections on the heart* in childhood. Acute tonsillitis, arthritis, chorea, purpuric spots and urticaria in children should always be considered an indication for examination of the heart. A study of the "threshold of organic disease" based on 542 first attacks in children less than 12 years of age, shows heart conditions in 292; chorea in 268; arthritis and arthritic pain in 267; tonsillitis and sore throat in 147; nervous symptoms other than chorea in 80; anemia in 78; abdominal symptoms in 52; cutaneous symptoms in 39; cachexia in 39; nodules in 22; epistaxis in 9, and nephritis in 2. Of the infectious lesions of the heart, Poynton finds that acute dilatation is rarely fatal of itself; myocarditis is usually associated with an hereditary tendency to rheumatism and is rarely fatal in the first attack; and pericarditis is a severe infection often associated with a fatal carditis. In 150 necropsies on children dying of carditis, the pericardium was adherent in 113 cases and normal in only nine cases.

Hall and Wilson²³ saw a case of *traumatic pericarditis* in a girl, 12 years of age, who had pinned a rusty needle in the front of her dress. Following an attack of vomiting and pain in the chest only half of the needle was found. Five days later she developed fever and signs of pericarditis with effusion. The roentgen ray showed the needle extending through the chest wall over the heart, and the pericarditis cleared up on removal of the needle.

Kinsella,²⁴ working on twelve cases of *subacute or chronic endocarditis* (endocarditis lenta), with bacteremia finds nonhemolytic streptococci in all of them. These organisms fall into two groups. *Streptococcus viridans* and *S. saprophyticus*, the latter being very indifferent for mice. Blood transfusions were tried, and in two cases where the sterile physiologic sodium chlorid solution used was not freshly made, severe febrile reactions occurred, and the blood was completely sterile in twenty-four hours. This seems to show that the reduction in the

21. Bost, T. C., and Neve, A.: *Lancet* **2**:552 (Oct. 26) 1918.

22. Poynton, E. J.: *Brit. M. J.* **1**:249 (March 2) 1918; *ibid.* 417 (April 13) 1918.

23. Hall, A. J., and Wilson, J. B. F.: *Lancet* **2**:856 (Dec. 8) 1917.

24. Kinsella, R. A.: *Arch. Int. Med.* **19**:367 (March) 1917.

bacteria is due to a reaction on the part of the patient rather than to the introduction of complementary substances or antibodies in the blood of the donor.

Tuley and Moore²⁵ report an uncommon case of *congenital endocarditis* in a boy, 13 years of age, where the pulmonary orifice was almost obliterated, the valves being covered with friable pendulous vegetations, and wart-like outgrowths filling the pulmonary artery. The foramen ovale is patent. In a review of the literature, only three cases were found in 2,400 medical admissions, with only one case diagnosed during life. Of 1,050 cases of valvular involvement, 0.01 per cent. have only the pulmonary valve involved. Malloch and Rhea²⁶ discuss endocarditis due to *Bacillus influenzae*, reporting two cases and reviewing the literature on the subject.

Aneurysm of the thoracic aorta is rare in children, only about twenty cases being on record. In Herman's²⁷ case, a boy 13 years old, with a four plus Wassermann, the electrocardiogram showed ventricular predominance. Bronson and Sutherland²⁸ report a case of aneurysm of the thoracic aorta in a child 6 years old, following a partial congenital stenosis of the ascending aorta. Rupture of the aneurysm caused death. Seven similar fatal cases are collected from the literature. Lutembacher²⁹ reports two cases of *aneurysm of the left auricle*, one in a young boy suffering from a mitral lesion which was followed by an infectious endocarditis. The roentgen ray showed the right border displaced 1 cm. to the right and the apex 1 cm. to the left. The left auricle at necropsy formed an aneurysmal sac containing 250 c.c. of blood.

Bacigalupo³⁰ reports what he believes to be the first case of *congenital cyst of the pericardium* on record. It is a pear-shaped tumor in the region of the left auricle which weighs 30 gm. It is a muco-dermoid cyst or fetal inclusion of epithelial cells in the third or fourth branchial clefts.

Aitken³¹ found a case of *congenital transposition of the heart* with the liver and spleen in the normal position.

F. Parkes Weber's³² case of congenital heart disease, probably a pulmonary stenosis, is one of the 10 or 20 per cent. of congenital heart lesions found associated with mongolian idiocy.

25. Tuley, H. E., and Moore, J. W.: *Am. J. Dis. Child.* **13**:426 (March) 1917.

26. Malloch, A., and Rhea, L. J.: *Quart. J. Med.* **12**:174 (April) 1919.

27. Herman, H.: *J. A. M. A.* **73**:292 (July 26) 1919.

28. Bronson, E., and Sutherland, G. A.: *Brit. J. Child. Dis.* **2**:241 (Oct. 15) 1918.

29. Lutembacher, R.: *Arch. d. Mal du coeur* **11**:434 (Oct.) 1918.

30. Bacigalupo, J.: *J. A. M. A.* **71**:961 (Sept. 21) 1918.

31. Aitken, R.: *Brit. M. J.* **2**:425 (Sept. 29) 1917.

32. Weber, F. P.: *Brit. J. Child. Dis.* **14**:269, 1917.

BLOOD TRANSFUSION

In cases of hemorrhage in the new-born, Lowenbury³³ transfused 80 c.c. of blood into the longitudinal sinus, going in through the posterior angle of the anterior fontanel. In addition 80 c.c. of blood were injected under the skin of the abdomen. The child was stuporous and dying at the time of the transfusion, but assisted by artificial respiration it recovered. This method of transfusion in infants was first used by Knox,³⁴ who mixed 50 c.c. of blood with 60 c.c. of a sodium citrate solution and injected 15 c.c. directly into the longitudinal sinus, and 95 c.c. intramuscularly. Later, Berghausen³⁵ introduced from 150 to 200 c.c. of citrated blood into the longitudinal sinus. Dunn³⁶ used the longitudinal sinus as a method for the intravenous injection of glucose in infants.

Vincent³⁷ uses a very simple and rapid method for obtaining the blood grouping for transfusion. Citrated serum (containing 1.5 per cent. sodium citrate) from Groups II and III is preserved with 0.25 per cent. tricesol. To test: a drop of Serum II is put at the left end of a slide, a drop of Serum III is placed at the right end, then two drops of the blood to be tested are obtained by a finger prick and placed between the drops of serum, a drop being mixed with each serum. Positive agglutination is shown by clumping and is seen macroscopically in less than one minute. The group number of the corpuscles is obtained by comparison with the result of combinations of reactions in the two middle columns in the table.

GROUP NUMBER OF CORPUSCLES					
Serum					
	I	II	III	IV	
I	0	+	+	+	I
II	0	0	+	+	II
III	0	+	0	+	III
IV	0	0	0	0	IV
	I	II	III	IV	

Robertson³⁸ preserves red blood cells from ten to twenty-six days, using them for transfusion as long as there is no hemolysis. He injects from 500 to 1,000 c.c. in cases that without transfusion seem hopeless. In twenty such cases, eleven patients were discharged improved, and two died.

33. Lowenbury, H.: J. A. M. A. **72**:1615 (May 31) 1919.

34. Knox, Jr., J. H. M.: Arch. Pediat. **34**:771, 1917.

35. Berghausen, O.: J. A. M. A. **70**:514 (Feb. 23) 1918.

36. Dunn, C. H.: Am. J. Dis. Child. **14**:52 (July) 1917.

37. Vincent, B.: J. A. M. A. **70**:1219 (April 27) 1918.

38. Robertson, O. H.: Brit. M. J. **1**:691 (June 22) 1918.

The work of Ashby³⁹ on the *life of the transfused blood cell* gives a new conception of the value of transfusion. She uses the blood of a recipient transfused with the blood of a group other than his own. The specimens are treated with a serum that agglutinates the recipient's corpuscles, leaving the donor's corpuscles free and unagglutinated. The count of these corpuscles indicates the amount of transfused blood still present in the recipient's circulation. The life of the transfused red corpuscle is thirty days and more. If this be uniformly true, then the stimulation of the bone marrow cells is brought about by the increased content of the circulation with its resultant improvement of metabolism rather than through the stimulating effect of cell debris.

Lindeman⁴⁰ estimates the *total blood volume in anemias*, by taking specimens from both patient and donor before transfusion by the syringe-cannula method, and a third specimen from the recipient three minutes after the transfusion is completed. These specimens of about 6 c.c. are collected in a calibrated centrifuge tube containing 0.2 c.c. of saturated potassium oxalate solution, shaken slightly, corked and centrifuged twenty minutes at 3,000 revolutions per minute. This determines the volume percentage of red and white cells. The amount of blood transfused is measured accurately. Then the total blood of the recipient is calculated by the formula $x = \frac{lb - bc}{a - 1}$

x = initial volume.

a = red blood corpuscle volume percentage of the initial volume.

b = volume of new blood given.

c = red blood corpuscle volume percentage of the blood given.

l = final red blood corpuscle volume content after transfusion.

COAGULATION TIME

Glycerinized extracts from the tissues of a 6 year old child who died of hemophilia, and from the tissues of a normal child killed in an accident, are studied by Lowenburg and Rubenstone⁴¹ in an attempt to ascertain the *effect of internal organs* on the coagulation time. The blocks of fresh tissue are ground up in sterile physiologic sodium chlorid solution, and brought to volume by the addition of glycerin. All the tissue extracts from both the normal and the hemophilic child, with the exception of the extracts of thyroid and liver, hasten the time of coagulation. Howel's method of oxalating the blood plasma, then reactivating coagulation by the addition of a suitable amount of calcium chlorid, so that the normal coagulation time is from 8 to 12 minutes, was used. The extracts of liver and thyroid prolong the

39. Ashby, W.: J. Exper. M. **29**:267, 1919.

40. Lindeman, Edw.: J. A. M. A. **70**:1209 (April 27) 1918.

41. Lowenburg, H., and Rubenstone, A. I.: J. A. M. A. **71**:1196 (Oct. 12) 1918.

time and even inhibit the action of calcium added to the plasma to produce a clot.

This finding acquires significance in the light of the discovery of *two new factors in coagulation*, heparin and proantithrombin, which have been isolated by Howel and Holt.⁴² Heparin is a phosphatid derived in largest amount from the liver. Its function is to activate proantithrombin, and to inhibit the conversion of prothrombin to thrombin. These new factors preventing coagulation safeguard the fluidity of the blood, preventing intravascular clotting. Variations in the amount of heparin may explain the variations in coagulation in hemophilia. Proantithrombin is isolated from blood plasma by precipitation with acetic acid, or ammonium sulphate added to half saturation. Heparin is thermostabile and proantithrombin is thermolabile.

Fornio⁴³ has a new *coagulovimeter* where the index of coagulation equals the ability of a given specimen to overcome the preventive action of a given quantity of magnesium sulphate. Sindoni⁴⁴ finds that the coagulation time is slightly retarded with a slight reduction in the viscosity of blood in children with pernicious anemia, chlorosis, kala azar, malaria and congenital heart disease. Shattuck⁴⁵ finds a marked delay in the whole blood coagulation time and in the prothrombin time during the attacks of serum sickness, with a return to normal following recovery.

BIOCHEMICAL AND BIOPHYSICAL STUDIES

The *sodium chlorid concentration* in Cannata's⁴⁶ studies on twelve normal infants varied in the first twenty-four hours from 0.392 to 0.434 per cent; within five days it was 0.460 per cent. Courtney and Fales⁴⁷ consider the sodium chlorid concentration in normal infants to be the same as in adults, but the total solids are lower. In tetany the chlorids and total solids are slightly higher; while in case of malnutrition and digestive disorders the chlorids are low, but the total solids tend to remain constant. Getter and St. George,⁴⁸ judging from 15,000 chemical analyses of bloods, claim that, except in conditions with complications in the excretory apparatus under which they include retention due to deficient blood circulation and retention due to production of large quantities of waste products of body protein as in

42. Howel, W. H., and Holt, E.: *Am. J. Physiol.* **47**:328 (Dec.) 1918.

43. Fornio, H.: *Cor.-Bl. f. Schweiz. Aerzte* **48**: (May 4) 1918; abstr. *J. A. M. A.* **71**:154 (July 13) 1918.

44. Sindoni, M.: *Pediatrics* **27**:278 (May) 1910.

45. Shattuck, H. F.: *Arch. Int. Med.* **20**:167 (Aug.) 1917.

46. Cannata, S.: *Pediatrics* **25**:641 (Nov.) 1917; abstr. *J. A. M. A.* **70**:64 (Jan. 5) 1918.

47. Courtney, A. M., and Fales, H. L.: *Am. J. Dis. Child.* **14**:202 (Sept.) 1917.

48. Getter, A. O., and St. George, A. V.: *J. A. M. A.* **71**:2033 (Dec. 21) 1918.

nephritis, cardiac disease, diabetes, furunculoses, carbuncles and gout, chemical analyses for nitrogen partition, creatinin, uric acid, sugar and alkali reserve have no diagnostic value. Even in pneumonias they could find no definite chlorid retention by blood examinations. They consider as normal blood values:

	Mg. Per 100 C.c. Blood
Nonprotein nitrogen	25 - 40
Urea nitrogen	10 - 18
Creatinin	1.1- 0.8
Uric acid	0.5- 3
Sugar	60 -110
Alkali reserve	53%-80%

The methods for the estimation of *nonprotein nitrogen* in the blood are still in a process of formulation with as yet no definite stabilization. The problem of removal of protein is one of the most discussed points. Greenwald⁴⁹ substitutes a 5 per cent. trichloroacetic acid for 2.5 per cent. trichloroacetic acid and kaolin. Morgulis and Jahr⁵⁰ object to the removal of ammonia by the air current, so after removal of proteins by precipitation they absorb the ammonia in the filtrate with permutit, and release it with sodium hydroxid. Then a measured quantity of ammonia is added to the filtrate to make it possible to read the color produced by nesslerization in the colorimeter. In six normal subjects there was from 0.27 to 0.14 mg. NH_3 per hundred gm. of blood. Gad-Anderson⁵¹ points out that the normal concentration of ammonia in the blood is low, and nearly constant, between 0.25 and 0.50 mg. per hundred c.c. of blood. Contrary to earlier observers, the ammonia content of muscle and blood are the same. Peters⁵² gives a method for the microdetermination of nitrogen by direct nesslerization and of total solids in drop quantities of human blood. For nitrogen a few drops of blood are distributed in a measured quantity of liquid medium and the total blood quantity is ascertained by weight; and for total solids, the blood is mixed with a suspension of dry weighed talcum powder, and is then dried and weighed. This method uses from 15 to 30 drops of blood for total nitrogen, nonprotein nitrogen and total solids.

The standards for the normal amount of *creatinin* and *creatin* are also undetermined. Greenwald and McGuire⁵³ point out that the picric acid method is probably inaccurate owing to the fact that in picric acid solutions exposed to light there are developed substances

49. Greenwald, I.: J. Biol. Chem. **34**:97 (April) 1918.

50. Morgulis, S., and Jahr, H. M.: J. Biol. Chem. **38**:435 (July) 1919.

51. Gad-Anderson, K. L.: J. Biol. Chem. **39**:267 (Sept.) 1919.

52. Peters, A. W.: J. Biol. Chem. **39**:285 (Sept.) 1919.

53. Greenwald, I., and McGuire, G.: J. Biol. Chem. **34**:103 (April) 1918.

giving color reactions similar to those of creatinin. Shaking dilute blood solutions with kaolin removes the creatinin, leaving creatin unaffected. The total creatinin (creatinin + creatin) is determined, then the creatin and the difference gives the amount of creatinin. A comparison of the normal in eleven individuals, using the Folin method and the new method, gives by the Folin method creatinin of from 1.12 to 2.2 mg. per hundred c.c., and by the new method from 1.00 to 2.45 mg. per hundred c.c.; creatin by the Folin method is from 2.93 to 4.99 mg. per hundred c.c., and by the new method from 1.40 to 3.73 mg. per hundred c.c. of blood. The diagnostic usefulness of these determinations is not established. Hunter and Campbell⁵⁴ find the total creatinin uniformly distributed in the corpuscles and plasma, and within the normal limits of 1.0 to 1.4 mg. per hundred c.c. given by Folin and Denis; but the creatin in the blood plasma is so far below the creatin in whole blood that there is no doubt that the bulk is in the red blood corpuscles. If the total creatinin is uniformly distributed, and the corpuscles contain from five and one half to ten times the amount of creatin in the plasma, then creatinin must predominate in plasma.

In determining the *calcium content of blood*, Howland and Marriot⁵⁵ use blood serum, while Cowie and Calhoun,⁵⁶ using Lyman's method,⁵⁷ point out the fact that calcium is present in appreciable amounts in the red blood corpuscles, so that the results obtained by different methods are not comparable without standardization.

Sedgwick and Kingsbury,⁵⁸ find that the *uric acid content* of blood of new-born infants increases from birth to a maximum of 3.9 mg. on the third day; then decreases to 2.9 mg. on the fifth day; to 1.6 mg. from the eighth to the eleventh day, persisting high until after fourteen months on a pure milk diet.

Benedict⁵⁹ makes slight modifications in the Lewis-Benedict method for determining *blood sugar*. Morgulis and Jahr⁶⁰ point out that creatinin gives the same reaction as sugar with the Lewis-Benedict reagent. In creatinin concentrations of 2 mg. per hundred c.c. of blood, the accuracy of the sugar determinations will not be influenced, but when in pathologic conditions the creatinin level may rise to from 10 to 40 mg. per hundred c.c., the Lewis-Benedict method loses its quantitative value.

54. Hunter, A., and Campbell, W. R.: J. Biol. Chem. **33**:169, 1918.

55. Marriott, W. McK., and Howland, J.: J. Biol. Chem. **32**:233, 1897.

56. Cowie, D. M., and Calhoun, H. A.: J. Biol. Chem. **37**:505, 1919.

57. Lyman, H.: J. Biol. Chem. **29**:169, 1917.

58. Sedgwick, J. P., and Kingsbury, F. B.: Am. J. Dis. Child. **11**:98 (July) 1917.

59. Benedict, S. R.: J. Biol. Chem. **34**:203 (April) 1918.

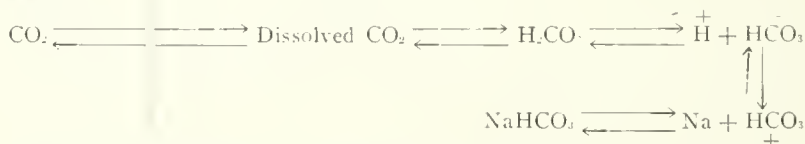
60. Morgulis, S., and Jahr, H. M.: J. Biol. Chem. **39**:119 (Aug.) 1919.

Dubin⁶¹ finds in experimental trypanosome anemia in dogs, that the *total lipoids* in the blood are increased, but lecithin and cholesterol are diminished. Csonka⁶² lists the lipoids in human blood as free fatty acids, glycerids, cholesterol esters, soaps and the radical of lecithin and phosphatid groups. The fatty acids in normal individuals are fairly constant. Palmitic and stearic acid and their soaps are not hemolytic, but oleic acid has a strong hemolytic action which is suggested as the cause of anemia in infections with *Bothriocephalus latus*. The unsaturated fatty acids of the blood are exogenous, endogenous and desaturated food and depot fat mobilized for transport. Forty-eight per cent. of the total fatty acid content, or 0.143 gm. per hundred c.c. of blood, are unsaturated fatty acids including oleic and both higher and lower fatty acids. In pathologic conditions the proportion of unsaturated fatty acids is generally higher than normal, and especially in diseases where the hemoglobin content is low, the iodine absorption power is increased.

The most important advance in studies on the blood has to do with the oxygen and carbon dioxide content and the relation to hydrogen ion concentration and alkali reserve. This opens an entirely new field, and materially changes our conceptions of the effect of anesthetics, the cause of shock and the effect of acid producing diets. Henderson and Haggard⁶³ emphasize the fact that the *balance between acids and alkalis* is one of the most important equilibriums of the living body, and it is never markedly altered until the organism is practically moribund. The alkaline reserve equals the carbon dioxide capacity. The physicochemical equilibrium is the balance of carbon dioxide against NaHCO_3 to H, that is C_H in the expression.

Pulmonary
Air

Blood



When by rebreathing or under morphine the carbon dioxide level is increased, the alkali level is correspondingly raised. Under ether the level of carbon dioxide and alkali are lowered. Henderson, Prince and Haggard⁶⁴ demonstrate that the lowering of the carbon dioxide level is

61. Dubin, H.: J. Biol. Chem. **33**:377, 1918.

62. Csonka, F. A.: J. Biol. Chem. **33**:401, 1918.

63. Henderson, Y., and Haggard, H. W.: J. Biol. Chem. **33**:333, 1918.

64. Henderson, Y., Prince, A. L., and Haggard, H. W.: J. A. M. A. **69**:965 (Sept. 20) 1917.

due to excessive breathing ventilating a large amount of carbon dioxide from the lungs, decreasing the carbon dioxide combining power of the blood, so that alkali passes out into tissues. This leaves the proportion of $\text{H}_2\text{CO}_3:\text{NaHCO}_3$ or C_H less altered. The critical value of carbon dioxide is from 33 to 36 volumes per cent. Below this all the vital functions are depressed. Excessive artificial respiration results in a decrease in the carbon dioxide capacity of the blood and in a lowering of arterial pressure. Henderson and Haggard,⁶⁵ checking Cannon's report that wounded soldiers in shock have a reduced alkali reserve or carbon dioxide capacity, succeeded in preventing experimental shock in dogs on handling the viscera, by giving inhalations of carbon dioxide.

Stillman and Cullen⁶⁶ use neutral red as the indicator for determining carbonates and bicarbonates in the absence of other buffer substances in the blood because neutral red shows a P_H value of 7.4 accurately. Phenolsulphonephthalein has uniformly a P_H value of 0.2 or 0.3 lower than neutral red. Stillman⁶⁷ compares the Van Slyke gasometer method for carbon dioxide capacity in blood, with the carbon dioxide titration method and finds that they agree within less than 2 millimoleculars of bicarbonate concentration in plasma. Van Slyke⁶⁸ gives a formula for the estimation of plasma bicarbonate based on the amount of acid and ammonia excreted in the urine per liter, per twenty-four hours.

$$\text{Plasma CO}_2 = 80 \sqrt{\frac{\text{D}}{\text{W}}} \sqrt{\text{C}}$$

D = c.c. of 0.1 N titratable acid and ammonia per twenty-four hour unit.
C = amount per liter.

Schloss and Harrington⁶⁹ compare the carbon dioxide tension in alveolar air, and the P_H concentration of urine with the bicarbonate of blood plasma. McClendon, von Meysenbug and Engstrand⁷⁰ show that the *alkaline reserve* in man and dog is remarkably resistant to changes in diet, an acid forming diet causing no change in the normal alkali reserve of 0.0335 N. in blood.

Studies on carbon dioxide tension and carbon dioxide capacity in the blood plasma are studies of the alkaline reserve or the acid-alkali balance. Normal blood contains buffer substances in solution which tend to lessen alterations in the hydrogen ion concentration when acids or alkalis are added. The buffer reaction varies with the pres-

65. Henderson, Y., and Haggard, H. W.: J. Biol. Chem. **33**:335, 1918.

66. Stillman, E., and Cullen, G. E.: J. Biol. Chem. **38**:167 (May) 1919.

67. Stillman, E.: J. Biol. Chem. **39**:261 (Sept.) 1919.

68. Van Slyke, D. D.: J. Biol. Chem. **33**:271, 1918.

69. Schloss, O. M., and Harrington, H.: Am. J. Dis. Child. **17**:85 (Feb.) 1919.

70. McClendon, J. F., von Meysenbug, L., Engstrand, O. J., and King, F. J. Biol. Chem. **38**:539 (July) 1919.

sure of carbon dioxid, according to Debenham and Poulton,⁷¹ so that the volume of carbon dioxid dissolved in 100 c.c. of blood is measured and the relationship determined between this and the hydrogen ion concentration. In the acidosis due to altitude, to exercise at an altitude and to cardiorenal disease it requires a smaller increase in carbon dioxid pressure to affect a given alteration in P_H value than it does in normal blood.

The subject of *oxygen tension and oxygen unsaturation* is an entirely different problem, associated, not with acidosis or with alkaline reserve, but with the combining power of the hemoglobin present. Debenham and Poulton⁷¹ report their findings on the *oxyhemoglobin dissociation curves* in normal men, without attempting to explain their values.

Harrop⁷² considers that an arterial oxygen saturation of 93 to 100 per cent. of the maximum capacity agrees with the values of the dissociation curves for oxyhemoglobin, but the tissues are able to take oxygen from the blood over a wide range of oxygen pressure. In cardiac disease the primary condition of the lungs has an important effect on the oxygen saturation of arterial blood during periods of decompensation. The normal oxygen consumption is 2.6 or 8.3 volumes per cent. In severe anemia he finds the oxygen saturation does not differ from the normal, while Lundsgaard⁷³ finds that there is a proportionality between the color index and the oxygen combining power, although unsaturation is independent of oxygen capacity, unless the capacity be reduced below the normal value for oxygen unsaturation. The tissues take from the blood all the oxygen they need regardless of whether a large reserve or no reserve at all of oxygen is left. Only after all the reserve oxygen is used is there an increase in the rate of circulation. When the hemoglobin falls below 30 per cent. the blood flow must be accelerated to provide a normal tissue oxygen supply.

The normal oxygen content of venous blood Lundsgaard⁷⁴ finds is about 13.6 volume per cent., with an oxygen unsaturation value of 5.8 volume per cent. In a series of studies on *cyanosis*⁷⁵ he finds that there is no relation between cyanosis and the carbon dioxid content of venous blood; cyanosis being associated with both high and low carbon dioxid values. The amount of oxygen in venous blood also bears no simple relationship to cyanosis, but there is an intimate relationship between the amount of oxygen unsaturation (the difference between

71. Debenham, L. S., and Poulton, E. P.: *Quart. J. Med.* **12**:38 (Oct.) 1918. (Jan.) 1919.

72. Harrop, Jr., G. O.: *J. Exper. M.* **30**:241 (Sept. 1) 1919.

73. Lundsgaard, C.: *J. Exper. M.* **30**:147 (Aug. 1) 1919.

74. Lundsgaard, C.: *J. Biol. Chem.* **33**:133, 1918.

75. Lundsgaard, C.: *J. Exper. M.* **30**:259, 271, 289, 295 (Sept. 1) 1919.

oxygen capacity and oxygen content per hundred c.c. of blood) and the degree of cyanosis. When the oxygen unsaturation is below 8 volumes per cent. there is no cyanosis; from 8 to 13 volumes per cent. there may or may not be cyanosis; but above 13 volumes per cent. there is always cyanosis.

In normal individuals the oxygen unsaturation is zero in the arteries, increasing in the capillaries to 5.5 volume per cent. in the veins, then decreasing in the lungs to zero — the oxygen unsaturation value in arterial blood. When the rate of reduction of oxyhemoglobin is increased in the peripheral capillaries, the increase in the venous unsaturation is more marked, going to 13.5 volume per cent. When the oxidation of hemoglobin in the lungs is incomplete, the arterial unsaturation may be 5.5 volumes per cent., increasing to 6.7 in the capillaries, and 8.2 volumes per cent. in the veins, returning in the lungs to the 5.5 per cent. in the arteries. In polycythemia the color is reddish, an erythrosis, rather than the blue of cyanosis, and has nothing to do with oxygen unsaturation. The secondary causes of cyanosis are incomplete oxidation of blood in the lungs, and increased oxyhemoglobin dissociation in the capillaries. When hemoglobin falls below 35 per cent., or an oxygen capacity of 6.5 volumes per cent., cyanosis cannot be produced.

Stadie,⁷⁶ using both arterial and venous puncture, determines the oxygen capacity, oxygen content and oxygen unsaturation. He finds the normal for five men at rest to be as follows:

Arterial oxygen content, from 17.9 to 22.1 volumes per hundred c.c. blood.

Arterial oxygen unsaturation, from 2.8 to 6.3 volumes per hundred c.c.

Venous oxygen unsaturation, from 22.7 to 33 volumes per hundred c.c.

In pneumonia cases the venous unsaturation is variable and has no prognostic value; while the arterial unsaturation in sixteen non-fatal cases of pneumonia showed a mean maximum of 13.9 volumes per cent. as compared with a mean maximum value of 32 volumes per cent. in sixteen fatal cases. Very rarely does a patient recover when the arterial oxygen unsaturation is over 20 per cent. The cause of cyanosis in pneumonia is an oxygen unsaturation. If methemoglobin were formed, the total oxygen would be reduced instead of increased as it is in all but very ill patients or fatal cases. The oxygen consumption or difference between the arterial and venous oxygen content is within normal limits in pneumonia.

76. Stadie, W. C.: *J. Exper. M.* **30**:215 (Sept. 1) 1919

RED BLOOD CORPUSCLES

The *viscometer* is used by Alder⁷⁷ to determine the volume of blood corpuscles, the average size of the separate cells, and the concentration of hemoglobin in the red corpuscles. Each red corpuscle carries the maximum quota of hemoglobin. The high color index in pernicious anemia is due to the increase in the size of the cells. The normal proportionate bulk of erythrocytes is from 42 to 46 per cent. The bulk of a single normal red cell averages 88 cubic microns. In pernicious anemia the average volume of a red corpuscle is from 119 to 165 cubic microns and in chlorosis it is 66 cubic microns.

Palmer⁷⁸ uses a colorimetric method for the determination of hemoglobin in which the standard solution is 5 c.c. of a 20 per cent. blood, made up to 100 c.c. with 0.4 per cent. ammonia solution and saturated with carbon monoxid. The unknown is diluted and saturated with coal gas. The accuracy is 1 per cent. Van Slyke⁷⁹ uses his gas apparatus, using the oxygen capacity as the basis for hemoglobin determination. The standard 100 per cent. hemoglobin has an oxygen capacity of 18.5 c.c. oxygen per hundred c.c. of blood. Appleton⁸⁰ checks the two methods showing that they are interchangeable and equally accurate, and determines the variation of hemoglobin percentage during infancy, using 103 normal children under 2 years of age, 90 per cent. of whom are breast fed. The results are best expressed by tabulation.

HEMOGLOBIN DETERMINATIONS IN 103 NORMAL CHILDREN

No. of Cases	Age	Maximum Hemoglobin, Per Cent.	Minimum Hemoglobin, Per Cent.	Average Hemoglobin, Per Cent.
12	1 day	192	141	164
14	2- 3 days	170	122	146
14	4- 8 days	157	122	135
8	9-13 days	174	114	137
16	2- 8 weeks	143	81	102
10	3- 5 months	103	75	88
17	6-11 months	111	73	87
12	11-23 months	94	60	85

In infants, then, there is a rapid decrease in hemoglobin during the first five or six months, which continues up to the second year, after which there is a rise to normal.

77. Alder, A.: *Cor.-Bl. f. Schweiz. Aerzte* **48**:1405 (Oct. 12) 1918; abstr. *J. A. M. A.* **71**:2028 (Dec. 14) 1918.

78. Palmer, W.: *J. Biol. Chem.* **33**:119, 1918.

79. Van Slyke, D. D.: *J. Biol. Chem.* **33**:127, 1918.

80. Appleton, V. B.: *J. Biol. Chem.* **34**:369 (May) 1918.

The *fragility of the red blood corpuscle* in thirty-seven cases of malaria studied by Netter⁸¹ is decreased during the malarial attacks; and this increased resistance is prolonged and augmented by quinin. Chaufford and Hubert⁸² recommend Ringer's solution for testing fragility because different isotonic saline solutions show variation in the hydrogen content, so they are not physiologic equivalents. The normal hydrogen ion content of the blood in twelve cases studied by Sonne and Jarløy⁸³ ranges from P_H 7.28 to 7.33.

Graham,⁸⁴ in a study of the acute form of *Banti's disease* found in children, reports a case in a girl, 7 years of age, where the maximal resistance of the red blood cell to varying hypotonic salt solutions was 0.26 per cent. where hemolysis is complete, and the minimal resistance 0.42 per cent. where hemolysis begins. He advises splenectomy before the onset of cirrhosis. Norris, Symmers and Shapiro⁸⁵ point out that since the pathologic changes found in spleens of 314 syphilitic subjects with cirrhosis of the liver are identical with the changes in Banti's disease, there is room for serious doubt whether Banti's disease is a true disease entity. Cannon, Frasier and Hooper⁸⁶ find that the red blood corpuscle count in cases of shock may show a capillary count as much as 2,000,000 higher than a simultaneous count from a vein. Continued capillary concentration is considered a bad sign.

Investigating the causes for the presence of *nucleated red corpuscles* in the peripheral circulation, Drinker, Drinker and Kreutzmann⁸⁷ find that in normal animals hard exercise does not dislocate nucleated red cells from the bone marrow, but that in anemic animals, with the increased circulatory content produced by severe exercise, there is an increase in the number of nucleated reds in the peripheral circulation, or a pseudocrisis. Section of vasomotor nerves, with dilatation of the vessels in the bone marrow, does not result in freeing nucleated reds from the marrow. A slight pseudocrisis⁸⁸ occurs immediately after saline infusion. True crises occur when there is a rapid regeneration of red blood corpuscles, usually the first week after hemorrhage.

81. Netter, L.: Rev. méd. de Bogota **37**:52, 1919; abstr. J. A. M. A. **73**:72 (July 5) 1919.

82. Chaufford, H., and Huber, J.: Presse méd. **26**:141 (March 18) 1918.

83. Sonne, C., and Jarløy, J.: Hospitalstid. **60**:1247 (Dec. 19) 1917; abstr. J. A. M. A. **70**:661 (March 2) 1918; Chem. Abstr. **12**:1893, 1918.

84. Graham, E. E.: Arch. Pediat. **33**:801 (Nov.) 1916.

85. Norris, C., Symmers, D., and Shapiro, L.: Am. J. M. Sc. **154**:893 (Dec.) 1917.

86. Cannon, W. B., Frasier, J., and Hooper, A. N.: J. A. M. A. **70**:526 (Feb. 23) 1918.

87. Drinker, C. K., Drinker, K. R., and Kreutzmann, H. A.: J. Exper. M. **27**:249 (Feb.) 1918.

88. Drinker, C. K., Drinker, K. R., and Kreutzmann, H. A.: J. Exper. M. **27**:383 (March) 1918.

ANEMIAS

Schneider,⁸⁹ in reporting seven cases, says that *aplastic anemia* implies a congenital defect in the form of poorly developed bone marrow which fails on demand for blood regeneration. Smith's⁹⁰ case in a boy, 6 years of age, seems to indicate from the splenic picture that the prolonged toxic action of measles acted in a culminative fashion until there was exhaustion of the bone marrow. Parkinson's⁹¹ patient recovered following two blood transfusions, the red count being as low as 580,000, with only one nucleated red seen.

D'Espine⁹² saw two infants, 5 and 11 months of age, respectively, with the true clinical picture of *pernicious anemia* who were treated with "hematopoietic serum" obtained by venesection from animals whose blood is at the height of regeneration following extensive bleeding. Both children recovered. Fifty-six cases of pernicious anemia in children are collected from the literature; thirty-two of these are due to bothrioccephalus or tenia. There are no verified cases of pernicious anemia in infants, and only two cases of essential progressive pernicious anemia in older children are established. Morse and Wohlbach⁹³ report a case in a child beginning at 5 years of age, and ending with death at eight years. *Ascarus lumbricoides* was found. The presence of hemosiderin granules in the urinary sediment should be an aid in the diagnosis of pernicious anemia. Raus⁹⁴ emphasizes the fact that urinary siderosis is a renal condition and not a renal disease. Wood⁹⁵ calls attention to the occurrence of *tropical sprue* in this country. The blood picture is a secondary anemia with a pernicious anemia color index. In the case reported the color index was 1.66, with marked variation in the size of the reds, macrocytes predominating, but microcytes were also present; poikilocytosis is noted, but there are no nucleated reds.

BLOOD PLATELETS

Thomsen⁹⁶ counts blood platelets from blood to which a little sodium citrate is added. On standing, the erythrocytes settle, leaving the plates floating in the plasma from which a direct count is made

89. Schneider, J. P.: Am. J. M. Sc. **156**:799 (Dec.) 1918.

90. Smith, L. W.: Am. J. Dis. Child. **17**:174 (March) 1919.

91. Parkinson, J. P.: Brit. J. Child. Dis. **16**:1, 1919.

92. D'Espine, A.: Rev. méd. de la Suisse Rom. **38**:461 (Aug.) 1918; abstr. J. A. M. A. **71**:1444 (Oct. 26) 1918.

93. Morse, J. L., and Wohlbach, S. B.: Am. J. Dis. Child. **14**:301 (Oct.) 1917.

94. Raus, P.: J. Exper. M. **28**:645 (Nov.) 1918.

95. Wood, E. J.: J. A. M. A. **73**:165 (July 19) 1919.

96. Thomsen, O.: Hospitalstid. **62**:169 (Feb. 5) 1919; abstr. J. A. M. A. **72**:1652 (May 31) 1919.

Pettibone⁹⁷ shows that the platelets are deficient in the blood of cases of hemorrhagic purpura; prothrombin is slightly diminished in pernicious anemia, and in myelogenous leukemias the prothrombin time is prolonged, although the coagulation time is within normal limits. Hirose⁹⁸ finds that the power of blood to cause vasoconstriction, after defibrination depends, with one exception, on the platelet count. The carotid of an ox is suspended and attached to a tambour which records the constriction. When the platelet count is under 100,000 per cu. mm. if any vasoconstriction is produced, it is slight. Janeway, Richardson and Park⁹⁹ find that uncoagulated blood, blood plasma and extracts of leukocytes and erythrocytes, have no constrictor action, but the extract of blood platelets contains a crystalloid substance which has a powerful vasoconstrictor effect. This substance has no relation to any of the factors concerned in coagulation.

LEUKOCYTES

Sellards and Baetjer¹⁰⁰ say that organized cells circulating in the blood are governed in their distribution by biologic rather than mechanical factors. Intravenous injection of bacteria and peptone cause a marked leukopenia, the polymorphonuclears collecting in the vessels of the viscera, especially those of the lungs and spleen, returning often in increased numbers to the peripheral circulation. Sudden changes in the leukocyte count may be due to a redistribution of existing cells, the leukocytes appearing at the beginning of leukocytosis being mature.

Jørgensen¹⁰¹ took *leukocyte counts*, in six girls from 14 to 15 years old, at four different intervals after the first incision in the ear. There was a wide variation, the counts immediately after the stab being high, an emotional leukocytosis. The differential count was not altered. Walker¹⁰² gives a formula for the index of resistance in acute inflammatory states in adults.

$$(T-10) \div (R-70) = I. R.$$

T=digits in thousandths place of the given leukocyte count.

10=digits in thousandths place of the high normal leukocyte count.

P=per cent. of polymorphonuclears in any given leukocyte count.

70=per cent. of polymorphonuclears in high normal leukocyte count.

I. R.=index of resistance.

97. Pettibone, D. F.: J. Lab. & Clin. M. **3**:275 (Feb.) 1918.

98. Hirose, K.: Arch. Int. Med. **21**:604 (May) 1918.

99. Janeway, T. C., Richardson, H. B., and Park, E. A.: Arch. Int. Med. **21**:565 (May) 1918.

100. Sellards, A. W., and Baetjer, W. A.: Bull. Johns Hopkins Hosp. **29**:135 (June) 1918.

101. Jørgensen, G.: Hospitalstid. **62**:432 (April 2) 1919; abstr. J. A. M. A. **72**:1712 (June 7) 1919.

102. Walker, O. J.: J. A. M. A. **72**:1453 (May 17) 1919.

A negative I. R. means a disproportionate increase in polymorphonuclear leukocytes, or that the severity of the infection is greater than the reaction. It might be worth while to test this formula for children substituting for 10 and 70, the high normal values for the given age. Milio,¹⁰³ comparing the blood of four normal infants with that of eleven infants with sepsis, finds that there is always a leukocytosis with infantile sepsis, but it is not always a polynucleosis.

Bachmann¹⁰⁴ demonstrates a special substance in the leukocytes of immunized animals, which fits these leukocytes to contend with the infection. The phagocytes from immunized animals show a specific phagocytosis even in vitro. Clough,¹⁰⁵ working independently on thirty-three cases of acute lobar pneumonia, finds that at the time of the crises and following, 85 per cent. show phagocytic activity in the leukocytes when treated with the homologous strain of *Diplococcus pneumoniae* and 79 per cent. show agglutination. In the serum from patients who die, the leukocytes show no phagocytic activity. The phagocytic activity differs from the opsonic index in that it concerns an active phagocytosis of a virulent pneumococcus organism which is not phagocytizable in normal human serum. The phagocytic activity develops in nearly all patients who recover; it parallels the protective power for mice, is specific and limited to the type of pneumococcus causing the pneumonia.

Using lampblack, McJunkin¹⁰⁶ finds that 5 per cent. of the mononuclear cells which are phagocytic for the carbon particles are derived from similar phagocytic cells in the endothelial lining of the blood vessels, and are not of myeloblastic or lymphoblastic origin, and should be called endothelial leukocytes.

Lymphocyte reactions form the basis for a series of papers in the *Journal of Experimental Medicine*, January, 1919. Taylor, Witherbee and Murphy¹⁰⁷ find that large doses of roentgen rays cause a sharp fall in the lymphocyte count which reaches its low point forty-eight hours after exposure. This is followed by a primary rise, a secondary fall and permanent recovery to normal. When the polymorphonuclears are affected, there is an initial rise followed by a decrease to below normal and then a return to normal. The return of the polymorphonuclears is complete before the lymphocytes are normal. Taylor¹⁰⁸

103. Milio, G.: *Pediatrics* **27**:33 (Jan.) 1919.

104. Bachmann, A.: *Rev. med. del Rosario* **9**:1 (March) 1919; abstr. *J. A. M. A.* **72**:1503 (May 17) 1919.

105. Clough, P. W.: *Bull. Johns Hopkins Hosp.* **30**:167 (June) 1918.

106. McJunkin, F. A.: *Am. J. Anat.* **25**:27 (Jan. 15) 1919.

107. Taylor, H. D., Witherbee, W. D., and Murphy, J. B.: *J. Exper. M.* **29**:53 (Jan. 1) 1919.

108. Taylor, H. D.: *J. Exper. M.* **29**:41 (Jan. 1) 1919.

finds a relative and an absolute lymphocyte increase in twenty-five out of thirty persons with a solar dermatitis. This is also the explanation for the higher lymphocyte count in Caucasians who have lived for some time in the Philippines. Nakahara¹⁰⁹ notes that there are large numbers of cells showing mitotic figures in the germinal centers of the spleen during regeneration after destructive injury by heat. It seems evident to him that the marked lymphocytosis caused by heat is due to an enhanced activity of the splenic germinal centers in their attempt at rapid repair. Luden¹¹⁰ finds that diet may increase the cholesterol in the blood, and when this occurs there is a weakening of the lymphoid defense.

LEUKEMIA

Hedenius,¹¹¹ studying leukemia, reports two cases which seem to show that hypererythrocytosis and hyperleukocytosis may be different manifestations, caused by the same irritant. Cowie and Calhoun,¹¹² using intravenous injections of nonspecific protein, find that more than one mesenchymal fundament may be stimulated by the same substance, so that both myelocytes and nucleated red blood cells appear in the circulation. That they do not always appear simultaneously may argue that the two fundaments are affected differently. With nonspecific protein therapy in cases of arthritis the most marked improvement occurred in those cases where there was a definite bone marrow response. Thro¹¹³ calls attention to the presence of unusual bone marrow cells corresponding to Türk's lymphoid marrow cells or Naegeli's myeloblasts in a case of *acute lymphatic leukemia* where the number of nucleated red corpuscles was equal to the number of leukocytes and the red corpuscle picture was that of pernicious anemia. Achard and Leblanc¹¹⁴ tabulate the acute fatal cases of leukemia, showing the relationships of the elements of the blood, and the reactions of the blood producing organs. Dedichen¹¹⁵ gives two cases of *atypical leukemia* in children, where the course resembled that of an acute infectious disease, and although organisms were absent from the blood during life, streptococci were found in the spleens at necropsy. A third case in a boy, 10 years old, with severe anemia

109. Nakahara, W.: J. Exper. Med. **29**:17 (Jan. 1) 1919.

110. Luden, G.: J. Lab. & Clin. Med. **3**:141 (Dec.) 1917.

111. Hedenius, I.: Svenska Läk. Sällsk. Handl. **43**:631 (Sept.) 1917; abstr. J. A. M. A. **70**:66 (Jan. 5) 1918.

112. Cowie, D. M., and Calhoun, H.: Arch. Int. Med. **23**:69 (Jan.) 1919.

113. Thro, W. C.: J. M. Res. **38**:385 (July) 1918.

114. Archard, C., and Leblanc, A.: Arch. d. mal. du cœur **11**:289 (July) 1918; abstr. J. A. M. A. **71**:856 (Sept. 7) 1918.

115. Dedichen, L.: Norsk Mag. f. Lægevidensk. **79**:1105 (Oct.) 1918; abstr. J. A. M. A. **71**:1949 (Dec. 7) 1918.

and the blood picture of an acute lymphatic leukemia had the thymic tissue replaced by a lymphosarcoma. Weber¹¹⁶ diagnosed a similar case of mediastinal leukosarcomatosis with a leukemic blood picture by the roentgen-ray shadow.

Inaba and Ohashi¹¹⁷ report a new microbody, oval in shape from 2.5 to 3.0 μ by from 1.5 to 2.0 μ in size, whose protoplasm is grayish white, homogeneous and not transparent with nucleoid corpuscles massed at the poles, which was found in freshly drawn blood, from a case of *acute myeloblast leukemia* after treatment with arsphenamin. It is suggested that this micro-organism was driven out into the circulation by the action of the drug.

Griffin,¹¹⁸ reviewing twenty cases from the Mayo clinic in which the spleen was removed following radium treatment for myelogenous leukemia, concludes that the duration of the disease is in no way influenced by splenectomy. Johnston,¹¹⁹ studying the blood changes after splenectomy in kala azar, finds a new type of cell during the first seven days after operation. These cells are the neutrophil polymorphonuclear leukocytes with the "horse-shoe nucleus." They are probably stored cells from the bone marrow and the blood forming tissues which are transformed into mature polymorphonuclear leukocytes in the circulating blood. They are intermediate forms between the myelocyte and the mature neutrophil polymorphonuclear cell. Sellards¹²⁰ finds that blood taken from cases of measles at different stages did not produce measles in eight susceptible individuals, even when injected intravenously.

HEMODYSTROPHIES

Pettaluga¹²¹ increases the field of blood diseases by including all cases showing a close, often hereditary, connection between the blood producing organs and the endocrine system. Under these he lists hemorrhagic diathesis, purpuras, hemolytic jaundice, paroxysmal hemoglobinuria, hemophilia and scurvy. These diseases are hemodystrophies, where the biochemic abnormalities predominate over the histopathologic changes.

The résumé of Dr. Holmes¹²² on the anatomy and physiology of the circulatory system covers a part of the literature published in 1917-

116. Weber, F. P.: Quart. J. Med. **12**:212 (April) 1919.

117. Inaba, I., and Ohashi, S.: Am. J. Dis. Child. **16**:1 (July) 1918.

118. Griffin, H. Z.: Med. Rec. **94**:1020 (Dec. 7) 1918.

119. Johnston, E. M.: China M. J. **33**:1 (Jan.) 1919; abstr. J. A. M. A. **73**:65 (July 5) 1919.

120. Sellards, A. W.: Bull. Johns Hopkins Hosp. **30**:257 (Sept.) 1919.

121. Pettaluga, G.: Arch. Espan. de Pediat. **2**:513 (Sept.) 1918; abstr. J. A. M. A. **72**:152 (Jan. 11) 1919; **72**:1530 (March 24) 1919.

122. Holmes, J. B.: Am. J. Dis. Child. **15**:278 (April) 1918.

1918 which is not included in this review. The monographic article of Lichtenstein,¹²³ summarizing in detail the history, feeding charts and blood picture in ninety-two prematurely-born children, unfortunately was not available for review.

123. Lichtenstein, A.: Svenska Läk.-Sällsk. Handl. **43**:1533 (Dec. 31) 1917; abstr. J. A. M. A. **70**:1046 (April 6) 1918.

ERRATUM

In the paper by Edwards A. Park, M.D., and Roy D. McClure, M.D., Baltimore, on the "Results of Thymus Extirpation in the Dog, with a Review of the Experimental Literature on Thymus Extirpation," published in the issue of November, 1919, after the word "growth" at the end of the tenth line from the bottom of page 475, insert the following:

"or development, and may be the direct cause of prolonged retardation of growth or development through the entrance of infection," etc.

The American Medical Association will pay thirty cents each for the following issues of the AMERICAN JOURNAL OF DISEASES OF CHILDREN: January, 1913; February, March, November and December, 1914; January and August, 1915; January, 1918; March and April, 1919. Address to AMERICAN MEDICAL ASSOCIATION, 535 North Dearborn Street, Chicago, Ill.

American Journal of Diseases of Children

VOL. 19

FEBRUARY, 1920

No. 2

THE ETIOLOGY OF ARTHRITIS DEFORMANS IN CHILDREN *

ALBERT H. BYFIELD, M.D.

IOWA CITY

That the deforming types of arthritis have been existing from earliest historic times can scarcely be doubted. In mummies exhumed from Roman tombs, the disease has been definitely recognized, as is, for example, described by Moore.¹ In the treatise of Sudhoff,² however, the declaration is made that the disease was extraordinarily common in Egypt and also among Germanic tribes along the Baltic, probably because of the dampness of the climate. In England, gout and chronic joint conditions have long been almost endemic, although the former is far less common now-a-days. On the continent, however, there was formerly less mention of the disease and Trousseau³ commented on its rarity. At present the disease is usually encountered sporadically, although Beek⁴ found a region in Siberia where from 6 to 46 per cent. of the population, chiefly children between 8 and 13 years, have a chronic osteoarthritis.

When one attempts to find reference to the disease in children in the early medical literature, one is struck with the almost complete lack of data on this subject. Whether this is owing to the fact that the disease did not exist in the first decade of life, which is unlikely, or whether such joint diseases were not carefully differentiated, cannot be stated definitely. Deforming arthritis does not receive mention in the *Kinderbuch* of Felix Wurtz,⁵ although reference is made to other joint affections. Meissner,⁶ in his pediatric bibliography with its list of titles of papers published previous to 1850, was also silent on

* From the Department of Pediatrics, College of Medicine, State University of Iowa.

1. Moore: Rheumatic Arthritis from a Roman Tomb, *Tr. Path. Soc. London* **31**:286, 1882-1883.

2. Sudhoff, K.: Translated by Stockman, F. J. *Ann. Med. History* **1**:111, 1917.

3. Trousseau: *Clinical Medicine*: New Sydenham Society **4**:408, 1871.

4. Beek, E.: Ueber Osteoarthritis Deformans, *Arch. f. Klin. Chir.* **86**:662 (March) 1918.

5. Wurtz, F.: Translated by Fox, A. L.: *An Experimental Treatise in Surgery*, 1656.

6. Meissner, F. L.: *Grundlage der Literatur der Pædiatrik*, Leipzig, 1850.

this subject. The first case in children is supposed to have been recorded by Cornil⁷ in 1864, and after him Charcot⁸ was able to refer to two cases in children less than 12 years of age. Barthez and Rilliet⁹ stated that gouty rheumatism was of such rarity in childhood that it might conveniently be passed over in silence. In the monograph of Moncorvo¹⁰ we find the first adequate treatment of the subject, although in the historical discussion this author is struck with the dearth of literature, and in correspondence with his teacher, Bouchut, was informed that the latter had not seen six cases in twenty years, wherefore, he made no reference to it in the fifth edition of his work. He also quoted Niemeyer (1869) who stated that infants enjoyed an absolute immunity from nodular rheumatism, one of the terms commonly applied to the disease under discussion. The difficulty at that time and previously in distinguishing the various types of hyperplastic joint disease in children, owing to the lack of the finer diagnostic tests, led to confusion on the subject, and this confusion, similar to that existing in the classification of the disease in adults, was mirrored in the terminology. Thus, while Charcot's¹¹ *rheumatisme noueux* was used by many, one encountered also the term "benign hyperplastic synovitis" in the article by Von Wahl¹² in Gerhard's *Handbuch*, and rheumatoid arthritis of English authors. Von Wahl stated that this disease was extremely rare in childhood and had been seen by him only following the acute polyarthritis of infectious diseases. In this country, reference was made by Louis Smith¹³ to a case of arthritis deformans seen in 1871, and he spoke of it as being "one of great rarity." Twelve cases were collected by Lacaze-Dori¹⁴ and a few of the more striking facts were mentioned, such as the self-limited nature of the affection and the better prognosis in children than in adults. Chlorosis, humidity and cold were considered as contributory etiologic factors. In his opinion, a cure took place after a period of about one year. From that time on occasional references to the disease appeared in the literature.

7. Cornil: *Memoire sur les Coincidences Pathologiques du Rheumatisme Articulaire Chronique*, Mem. d. l. Soc. d. Biol. **1**:3, 1864 (Fourth Series).

8. Charcot: *Lecon Cliniques sur les Maladies des Viellards et les Maladies Chroniques* (1866), Paris **8**:262, 1890.

9. Barthez and Rilliet: *Maladies des Enfants* **2**:114, 1866.

10. Moncorvo: *Estudo Sobre o Rheumatismo Chronico Nodosa na Infancia e seu Tractamento a Proposito de uma Caso Observado em uma Menina de 2 annos, etc.*, Rio De Janeiro, 1879.

11. Charcot: See reference No. 8.

12. Von Wahl: *Gerhardt's Handbuch der Kinderkrankheiten* **6**:416, 1880.

13. Smith, L.: *A Treatise on the Diseases of Infancy and Childhood*, 1876, Ed. 3, p. 309.

14. Lacaze-Dori: *Etude Clinique sur la Rhumatisme Noureux Chez Les Enfants*, Thèse de Paris, No. 329, 1882.

A new interest was aroused by the masterly treatise of Still¹⁵ with its report of cases of chronic joint disease of a special type. Still wrote of a chronic progressive enlargement of the joints and enlargement of the glands and spleen, the onset usually taking place before the period of second dentition. The tissue change seemed to be around the joint rather than in it. In Still's cases the hands were rarely involved. Muscle wasting took place early. It seemed impossible, according to him, to find a definite cause for the slight fever which usually existed. Adherent pericardium was noted in five cases. It is important to emphasize the fact that the author clearly understood that he was not dealing with rheumatoid arthritis which also occurred in childhood and which resembled the rheumatoid arthritis of adults, for the term "Still's" disease has been applied rather loosely to all cases of chronic arthritis and peri-arthritis of childhood.¹⁶

Reports of cases of deforming arthritis of the type described by Still commenced to appear after the publication of the original article. Koeppe¹⁷ spoke of three cases which showed pericardial adhesions, and in the one case which came to necropsy no evidence of tuberculosis was found. Weber¹⁸ believed that Still probably took too gloomy a view of the prognosis. Valvular disease was present in his cases, but no cultures were obtained from the joints. In one case, a positive reaction was obtained with Koch's tuberculin. In Edsall's¹⁹ case a positive tuberculin reaction was obtained, and tubercle bacilli were found in the lymph nodes.

Poncet,²⁰ as a result of studies made since 1897, believed that chronic arthritis was the consequence of a general and attenuated infection, and that these larval infections might have their beginning in infancy or adolescence, and while they might be caused by syphilis, nevertheless, the most common cause must be tuberculosis. This conception of a "rheumatisme tuberculeux" has been the subject of lively controversy, but has not found general acceptance. Garrod²¹ and

15. Still, G. F.: On a Form of Chronic Joint Disease in Children. *Med. Chir. Tr.*, Edinburgh **80**:47, 1897.

16. In the Surgeon-General's Catalogue, all cases of arthritis deformans were classified under the heading "Still's Disease."

17. Koeppe, H.: *Jahrb. f. Kinderh. u. Physische Erziehung*, Vienna and Leipsic **76**:707, 1912.

18. Weber, F. P.: Still's Type of Chronic Joint Disease in Children and the So-Called Tuberculous Rheumatism, *Brit. J. Child. Dis.* **2**:208, 1905.

19. Edsall, D. L.: Concerning the Nature of Still's Type of Chronic Poly-arthritis in Children, *Arch. Pediat.* **21**:175, 1904.

20. Poncet: *Arthrites Chroniques et Rheumatisme Tuberculeux*, *Presse m d.* **21**:244, 1913.

21. Garrod: *Allbutt's System of Medicine*, Ed. 2, **3**:17, 1908.

Ibrahim²² express special doubt as to the justification of regarding "Poncet's disease" as a separate clinical entity.

The same difficulties, although possibly in less degree, have been encountered in attempts at classification. Rachford²³ mentions three types: the first, with hypertrophic changes predominant; the second, with atrophic changes prominent, and the third, Still's disease. One of the most complete clinical studies of the disease is that of Spitzky.²⁴ He reports cases and gives an excellent bibliography.

The question of the etiology of arthritis deformans in children has gone through the same stages of development as it has in adults. For a long time, and in spite of the fact that acute arthritis had been known to belong to a group of metastatic phenomena following tonsillar infection, chronic joint troubles were believed to be due to metabolic disturbances, although Still considered the possibility of infection as a cause of the type of disease which he observed. In addition to errors in metabolism, the nervous system and the ductless glands were also considered in attempting to assign a cause of the disease.

Royal Whitman,²⁵ in an interesting philosophical discussion of the disease, stated that "if rheumatoid arthritis is to be considered as of infectious nature, its distinction over ordinary forms of infection, whether local or general, is certainly marked. . . . One must presuppose a focus of infection within the body which is constantly active." Billings²⁶ and his co-workers were among the first to put this view into practical application. Rosenow²⁷ examined the lymph glands which drain the affected joints and found streptococci in them. He also found endothelial proliferation of the blood vessels which might have led to the trophic changes commonly seen. Lindsay²⁸ reported nineteen cases of rheumatoid arthritis in children and emphasized foci of infection as being etiologic factors. While he recommended that there should be a systematic examination of all the orifices of the body—mouth, nose, ears, rectum and vagina—and urged that the infected focus, if found, be eradicated, he did not say that by such eradication the patient was benefited.

22. Ibrahim: *Handb. d. Kinderh.*, Pfaundler and Schlossmann, Ed. 2 **2**: 401, 1910.

23. Rachford: *Diseases of Children*, 1912, p. 408.

24. Spitzky: *Zur Chronischen Arthritis der Kinder*, *Ztschr. f. orthop. Chir.* **11**:699, 1903.

25. Whitman, R.: A Report of Final Results of Two Cases of Polyarthritis in Children of the Type First Described by Still, Together with Remarks on Rheumatoid Arthritis, *Med. Rec.* **63**:601, 1903.

26. Billings, F.: Chronic Focal Infections and Other Etiological Relations to Arthritis and Nephritis, *Arch. Int. Med.* **9**:484 (April) 1912.

27. Rosenow, E. C.: Etiology of Arthritis Deformans, *J. A. M. A.* **62**:1146 (April 11) 1914.

28. Lindsay, J.: Rheumatoid Arthritis in Children, *Edinburgh M. J.* **10**:332, 1913.

Hammond's²⁹ experience with tonsillectomy in arthritis deformans did not lead him to feel encouraged as to the effectiveness of this operative measure. This is in accord with our own experience. A possible relationship between sinus infection and arthritis deformans in adults has been assumed by workers following the suggestions of Billings and his co-workers. The results of operation on the sinuses have not been uniformly satisfactory. It is interesting to note that chronic sinusitis was found in one instance in a series of cases of arthritis deformans in swine studied by Segikuchi and Irons.³⁰

Experience in this clinic³¹ early demonstrated that mere removal of the tonsils and adenoids was not sufficient to control the symptoms and signs of the disease, or to arrest its progress; therefore, it became necessary to institute a search for another focus of infection, especially as it was usual for such manifestations as slight elevations of temperature, leukocytosis, exacerbations of pain and even involvement of new joints to persist. No trouble was found in the teeth in the cases studied, and attention was then directed to the nose and especially to the accessory nasal sinuses, the details of the work being reported elsewhere by Dr. L. W. Dean,³² whose investigations and operations have made this article possible. A brief summary of the cases studied since 1916 is appended herewith.

REPORT OF CASES

CASE 1.—D. M., aged 5 years, was admitted in September, 1916, having had "joint" trouble for two years previously. In this case the spleen was palpable. Elbows, hips, ankles, dorsal spine and to some extent the hands and fingers on both sides were involved. The tonsils and adenoids were removed two months after admission, but improvement was extremely slow and a few slight exacerbations were noted. Sinus operation was not done because at this time the relationship between nose infection and joint trouble was not realized. After three years there was a distinct recurrence of the trouble. The patient now shows distinct evidence of chronic infection which can only be situated in the nasal sinuses as present examination shows.

CASE 2.—J. B., aged 1½ years, had been ill four months before admission to the hospital in May, 1917. The onset of the disease was subacute, the arms, elbows and knees being involved. The spleen was not palpable, and no lymph glands were felt. The joints were distinctly tender, and there was painful

29. Hammond, R.: The Rôle of the Nose, Throat and Accessory Sinuses in the Etiology of Chronic Infectious Arthritis, *J. A. M. A.* **65**:1091 (Sept. 25) 1915.

30. Segikuchi and Lyons: Chronic Arthritis in Swine, *J. Infect. Dis.* **21**:526 (Dec.) 1917.

31. Byfield, A. H.: Systemic Manifestations of Chronic Nasal Sinus Infection in Childhood, *J. A. M. A.* **71**:511 (Aug. 17) 1918.

32. Dean, L. W.: Infections of the Paranasal Sinuses in Infants and Young Children with Special Reference to Adenoids and Chronic Tonsillitis as Etiologic Factors, *Ann. Otol., Rhinol. & Laryngol.* **27**:534 (June) 1918; Dean, L. W.: Nasal Sinus Disease in Infants and Young Children, Including Bacteriologic Study, *Ann. Otol., Rhinol. & Laryngol.* **28**:454 (Sept.) 1919.

limitation of motion. A leukocytosis of 21,800 was observed. The highest temperature noted was 99.8 F. Three weeks after admission an operation for removal of tonsils and adenoids was performed. Improvement was very marked and rapid and by July 11 (five weeks later) pain and tenderness had practically disappeared. Some ankylosis persisted. There were no recurrences.

CASE 3.—J. N., male, aged 11 years, had been sick fourteen months before coming to the hospital in July, 1917. The onset was subacute, and at the time of admission the spleen was not felt. There was marked pain on handling, marked deformity and limitation of motion of many joints. The test for tuberculosis was practically negative. Six months after admission, the tonsils and adenoids were removed, but the benefit was not great. Seven weeks later a nasal sinus operation was performed and a very striking diminution of pain was observed in less than one week. The anorexia so often present in these cases diminished and the patient's general health improved. A second operation on the nasal sinuses was found necessary three months following the first. Again, improvement was noted within a day. From that time until the present there has been no exacerbation, and the patient, while still having bony deformity, must be regarded as having had his trouble definitely arrested. An older brother, not treated, is in an unbelievably crippled condition.

CASE 4.—F. R., aged 7 years, had been ill three years before admission in September, 1917. The onset was with sore throat, with progressive involvement of the joints following this. On admission there was torticollis, the cervical lymph glands enlarged, the spleen was very slightly palpable but not reaching beyond the costal margin, and there was marked involvement of many joints with swelling, deformity, limitation of motion and distinct pain on handling. The tonsils were removed three weeks after admission. Following this operation only slight improvement was noted. The sinuses were operated on only a short time after the tonsil operation. In this case the temperature elevation persisted, rising as high as 103 F. with a leukocyte count of 25,000. When the child was seen again about six months later, the fever had disappeared and no acute or subacute condition was present in the joints. A final observation in 1919 showed that the disease was distinctly arrested with only a residue of joint involvement undergoing orthopedic treatment. In this case, the operation on the nasal sinuses did not give as quick results as were seen in other cases, but the benefit to the joints was very great. The final result must be regarded as eminently satisfactory in view of the fact that there was a complete cessation of the recurring attacks, together with a partial return of function. The fact that the temperature elevation persisted even after the sinus operation suggests that a complete removal of infected tissue was not effected.

CASE 5.—M. R., aged 9 years, was admitted to the hospital in October, 1917, after seven years of recurring joint attacks. The usual findings of joint deformity and tenderness were present. The tonsils and adenoids were removed and sinus operations were done on the same day, and while there was a marked improvement, it was impossible to clear up the nasal infection even six months after admission. The patient, however, was without joint trouble for nearly two years, when he was readmitted with a recurrence. It should be mentioned, however, that in addition to the arthritis deformans, there were present a nephritis and a recurring colitis as complications. Furthermore, the child reacted very strongly to the intradermal tuberculin test. We must regard this case as one in which the patient was benefited but not cured. The complicating infection may have been responsible for the unsatisfactory result.

CASE 6.—F. B., aged 12 years, was sick one year before admission to the hospital in July, 1917. This case is reported mainly to emphasize the fact that removal of the tonsils and adenoids is insufficient to control the disease. This patient had only one or two of the larger joints involved and because of improvement in his general condition following the removal of the tonsils and adenoids, with arrest of the arthritic process, he was discharged, as it was

believed that the respiratory infection had worn itself out. The incorrectness of our assumption was shown by the fact that the patient returned to the hospital seven months afterward with many joints involved and with much resultant crippling. Operation on the sinuses was performed but the boy was removed from the hospital before it was possible to determine the permanent benefit obtained, although the immediate improvement was striking. In the light of our experience during the past three years, it seems fair to believe that had more radical treatment of the nose been instituted at once, spread of the disease could have been prevented.

CASE 7.—W. F., aged 11 years, had been sick three years before coming here in July, 1918. The onset was insidious. Few joints were involved and the existing deformity was slight. An incomplete tonsillectomy had been performed two years before admission and it was necessary to remove the tonsil stumps. This last operation was followed with infection of some joints previously free. Pain on handling and limitation of movement were quite constantly present during the three months that the patient was under observation. Frequent examinations were made. Operation on the nose was then done, following a submucous resection and this was followed in a week by unmistakable local and general improvement; from this period until the present there has been no recurrence and the patient has needed only orthopedic correction of the deformity already present.

CASE 8.—E. T., aged 3 years, was sick four months before admission in November, 1918, beginning with tonsillitis and marked multiple joint involvement, with very distinct tenderness and deformity. Tonsillectomy was performed shortly after admission, and the patient has had no recurrence after one year. The improvement was rapid and continuous.

CASE 9.—H. H., aged 8 years, when admitted in March, 1919, had been sick one year previously. The onset in this case was rather sudden, following tonsillitis. Few joints were involved, but there was trouble in the wrist and in some of the small bones of the left hand. A tonsil operation had been done; but, one year after this it was necessary to have the tonsil stumps removed and a nasal sinus operation was performed at the same time. There was moderate improvement for four months when there was a recurrence and a torticollis developed in addition to trouble in the hand and in the foot. The girl was put in bed and observed for nearly a month. A cast was applied to the foot, but the condition remained unchanged. While the distress and pain were not great, it was continuous and distinctly affected the girl's general health. There was limitation of motion in the neck and pressure on the hands was painful enough to cause crying. A second and more complete nasal operation was then done, and within a few weeks the torticollis had entirely disappeared, movement of the hands was possible, with practically no pain and the foot was much improved. The effect of this operation on the general health of the patient was a surprising one, even to those who have had occasion to share in the observations made in the past.

CASE 10.—I. H., aged 3 years, was sick one year before admission to the hospital in March, 1919. The tonsils and adenoids were removed and this was followed with rapid improvement and no recurrence.

DISCUSSION

In these patients a uniformity in the constitutional signs and symptoms was manifest, there being present emaciation of varying degree, anorexia and irregularity of temperature with frequent rises to 100 F. and occasional rises to 103 F. A leukocytosis of from 11,000 to 25,000 was present. At the time of admission to the hospital the spleen was

practically never found to be enlarged. A positive tuberculin test was seen in one case only. A rheumatic history was obtained in a few cases, but in only one instance (Case 3) was more than one member of the family similarly affected. The teeth were examined in every case and only once were they found to be diseased. No benefit followed extraction. Blood cultures were taken in two cases and were negative.

The disease tended to have its onset in the larger joints, usually the knee or the ankle, while the bones and articulations of the wrist were affected later. In two patients the affection remained monarticular for so long a period as to suggest a diagnosis of tuberculosis of the joints. With the progress of the disease to other joints the true nature of the trouble was indicated and appropriate treatment instituted.

The cases under discussion, therefore, do not appear to belong to the group described by Still, but resemble more nearly those cases which are commonly referred to as rheumatoid arthritis. In one case (Case 5) a very positive Mantoux reaction was obtained so that a diagnosis of Poncet's disease might have been considered. Since, however, two operations on the sinuses were followed with a subsidence of joint swelling and pain, it seems more probable that we were dealing with a case of deforming arthritis in an individual affected with tuberculosis. Convalescence in this case was slower than in most of the others; it may be possible that the presence of the tuberculous infection tended to delay improvement. In view of the fact that there has been considerable discussion as to the nature of Poncet's disease, this case is worthy of note.

There is no great choice of therapeutic measures in arthritis deformans in children if the infectious nature of the disease is admitted and if it is granted that the accessory sinuses of the nose are the commonest seat of the etiologic focus. General supportive measures, with orthopedic treatment of the joints alone, produce too little and too slow improvement to be regarded as efficacious. Furthermore, an extension of the disease cannot be thus avoided. Removal of the tonsils and adenoids is followed by slow improvement, but does not guarantee that there will not be a relapse. Intravenous and intramuscular injection of foreign proteins has not been made here, except in two cases (Cases 3 and 6) and in neither of these was the improvement striking. That one injection was not sufficient to prevent a very marked extension of the disease was shown in Case 6. It should be stated, however, that without a more careful trial, a definite opinion cannot be given. In the children in this series less than 3 years of age, removal of the tonsils and adenoids alone has seemed to be sufficient to cure and arrest the progress of the disease. It appears, therefore, that the younger patients with this malady may be spared nasal intervention. In older children, however, removal of the tonsils and

adenoids is definitely insufficient to accomplish this end, and in them the surgical intervention on the nasal sinuses, as practiced by the nose and throat department, is indicated and has yielded results which are eminently satisfactory.

It will be admitted that in estimating the benefits following on operative treatment of the nose, there is a considerable personal element: improvement, like beauty, may be in the eye of the observer. Past experience, however, with cases of arthritis deformans which were treated expectantly, with plaster casts, or by tonsillectomy, made tolerably clear the fact that where improvement did take place, it was slow and slight. It was this observation which led to the request that a search be made for other possible foci of infection, since it was believed that the older methods of treatment were unsatisfactory.

In spite of the fact that the disease has been termed a periarthritis from a pathologic standpoint, there is little question that the joint tissues adjacent to the cartilage show an extensive involvement,³³ and it can scarcely be expected, therefore, that a complete restitution to normal is possible, especially when the disease has existed for a number of years. Furthermore, the difficulty of complete elimination of foci of infection is also undeniable. When, however, nasal operations were almost invariably followed within a week by unmistakable subsidence of symptoms and signs, when "flare ups" occurred, if at all, only at very long intervals, when a very rapid improvement was noted in the general health of the child as well, it could scarcely be denied that there must be some direct connection between the operation and the improvement achieved. The results were immeasurably better than were those following the usual methods of treatment.

It should be borne in mind, also, that orthopedic treatment is definitely indicated where marked deformity and marked joint pathology exists, but the extent to which restitution may take place when the infection is controlled, is surprising even if casts are not applied. Five patients have been free from recurrence for at least two years.

CONCLUSIONS

From a study of the cases reported it may be concluded that:

1. Arthritis deformans in children results chiefly from a chronic infection situated in the tonsils and adenoids and in the accessory sinuses of the nose.
2. In children less than 3 years of age the portal of infection seems to be limited to the tonsils and adenoids. After this time removal of tonsils and adenoids is ineffective in arresting the progress of the disease.

33. Axhausen: Die Deformierende Gelenkentzündung (Arthritis Deformans) Im Lichte Neuer Forschung, Berl. klin. Wchnschr. 52:1205, 1915

3. A sinus infection should be suspected as an etiologic factor if, after the tonsils and adenoids are removed, there remains elevation of temperature (even if slight), leukocytosis, poor appetite, together with a slowness of the joints to become less painful and swollen. Relapse and exacerbations are definite indications of the need of nasal treatment.

4. Poncet's disease is probably no more than arthritis deformans in an individual infected with tuberculosis.

5. Although supportive and orthopedic measures are helpful, surgical treatment of the nasal sinuses is to be regarded as the most important therapeutic measure indicated in arthritis deformans in children.

6. The prognosis in uncomplicated cases is good as far as arrest of the disease is concerned. The deformity and functional disability may persist for a considerable time.

CALCIUM METABOLISM OF INFANTS AND YOUNG CHILDREN, AND THE RELATION OF CALCIUM TO FAT EXCRETION IN THE STOOLS*

L. EMMETT HOLT, M.D.

ANGELIA M. COURTNEY AND HELEN L. FALES

NEW YORK

PART I. INFANTS TAKING MODIFICATIONS OF COW'S MILK

Recently a large number of stools from children who were receiving food of a varied character were collected for a study of fat metabolism of infants and young children. In nearly all of this material total ash and calcium determinations were made. It was believed that the large number of observations made would furnish data of value in answering some much debated questions regarding calcium metabolism, especially in its relation to fat metabolism.

Many investigators have published data and have advanced theories on this subject, but the conclusions reached are contradictory and in many cases the observations on which they are based are very few in number. For example, the observations made on one breast fed infant for a single period and on one child fed on cow's milk, also for a single period, are quoted in nearly every article on this subject, and have been taken as standards for normal calcium metabolism.

Many diverse views are prevalent in regard to calcium metabolism. Some writers believe that a liberal intake of calcium results in an excessive excretion of calcium which is accompanied by a harmful loss of fat. Others hold that a high fat intake induces a large fat excretion, accompanied by a serious loss of bases, especially calcium. Both these dangers are supposed to be associated with occurrence of soapy stools. The German literature especially has emphasized the pathologic significance of large light-colored crumbly stools rich in calcium soaps and calcium phosphate, a type of stool apparently not so frequently seen in this country. There are still other writers who think that a large intake of calcium leads to a storage of calcium in the body which may have injurious effects. On the other hand, there are many who believe that an ample intake of both fat and calcium produces only beneficial results. It is generally accepted that cod liver oil has a

*From the Laboratories of the Rockefeller Institute for Medical Research and the Babies' Hospital, New York.

beneficial effect on the retention of calcium, but this opinion seems to be not entirely unanimous. The literature on all these questions is so voluminous that there is not space here to discuss it in detail.

The points of general interest in regard to calcium metabolism may be stated in the form of the following questions.

1. What is the normal excretion and absorption of calcium by children taking (a) modifications of cow's milk, (b) mixed diet?

2. How is the calcium excretion and absorption affected by the amount of (a) the calcium intake, (b) the fat intake?

3. Is there any evidence that either an excessive calcium intake or a very small calcium intake is harmful?

4. Is there any relation between the age or the weight of the child and the amount of calcium absorbed normally?

5. Is there any constant relation between the excretion of calcium and the excretion of fat in the form of soap?

6. Is there a serious loss of calcium in soapy stools?

7. On what is the calcium percentage of the total solids of the stool dependent?

8. How do the calcium excretion and absorption differ from normal when children are suffering from (a) diarrhea, (b) chronic intestinal indigestion, (c) active rickets or (d) when recovering from rickets?

9. What is the effect on calcium metabolism of (a) cod liver oil, (b) of vegetable fats?

In the observations reported in this and a subsequent paper on this subject the period of stool collection and the amount of food intake were exactly known. Thus, it was possible to determine closely the amount of calcium excreted and absorbed daily. In most of these cases values for the urinary excretion of calcium were not obtained. Hence, the actual *retention* of calcium is not reported. However, the *absorption* is practically the same as the retention, since the excretion of calcium in the urine of infants and young children is normally very small in amount. Previous work done in this laboratory has shown a general range of from 0.01 to 0.05 gm. of calcium oxid (CaO) excreted daily in the urine of infants taking modifications of cow's milk and from 0.03 to 0.15 gm. for children taking a mixed diet. With the small number of breast fed infants for whom values have been obtained, the urinary excretion of calcium was found to be from 0.014 to 0.026 gm. of calcium oxid daily. Rachitic children were found to excrete even less calcium oxid in the urine than did normal children of the same age. By calcium *excretion* is meant the total amount of calcium lost in the stools. Whether part of this calcium has been absorbed and subsequently excreted into the large intestine, as is believed by many to be the case, is not taken into consideration.

TABLE 1.—NORMAL INFANTS. RELATION OF ABSORPTION OF CALCIUM TO CALCIUM AND FAT INTAKE

No.	Case	Age in Mos.	Weight in Gm.	Stools	Intake of CaO Gm. per Kg.	CaO Absorbed Gm. per Kg.	Per cent. of Intake absorbed	Intake of Fat Gm. per Kg.	Grams of CaO Intake per Gm. Fat Intake	Remarks
113	J. S. 1	7.5	4,040	Nonhomogeneous	0.488	0.039	29.2	6.6	0.071	Skimmed milk with large amount of olive oil
72	A. K.	5.5	3,910	Constipated	0.297	0.133	44.8	5.6	0.053	
55	J. F.	12	5,485	Normal	0.285	0.131	46.1	5.2	0.055	
65	P. D. 3	7.5	4,884	Constipated	0.285	0.068	23.8	4.9	0.058	Rather high carbohydrate in diet
54	R. C.	8.5	6,290	Normal	0.283	0.124	43.8	5.2	0.051	High calories per kilogram
86	J. M.	4	3,402	Softnormal	0.279	0.098	35.3	3.7	0.076	Dried milk formula
158	H. B.	13	3,402	Normal	0.266	0.043	16.3	5.0	0.053	Very large stools
57	M. S. 2	8	6,145	Normal	0.264	0.123	46.6	4.8	0.052	
70	P. D. 1	7	4,635	Constipated	0.264	0.005	38.5	4.9	0.053	Rather high carbohydrate in diet. High calories per kilogram
71	P. D. 2	7	4,679	Constipated	0.257	0.030	11.7	4.8	0.053	Rather high carbohydrate in diet. High calories per kilogram
82	P. F.	4	5,055	Nonhomogeneous	0.235	0.099	42.0	3.1	0.076	Dried milk formula
97	B. W. 1	15	5,873	Softnormal	0.231	0.117	50.8	4.7	0.049	Recovering from multiple fractures. Very low calories per kilogram
85	C. M.	2	3,154	Nonhomogeneous	0.229	0.116	50.7	4.2	0.055	
106	A. A.	7	3,489	Nonhomogeneous	0.224	0.063	28.2	3.3	0.068	Very high proportion carbohydrate in diet
63	F. N. 2	11	5,806	Softnormal	0.222	0.063	11.9	4.2	0.051	High carbohydrate in diet. High calories per kilogram
60	F. N. 1	11	5,620	Constipated	0.217	0.090	15.1	4.7	0.047	High calories per kilogram
62	J. M.	7	5,500	Normal	0.204	0.063	30.8	4.2	0.049	Recovering from rickets. Taking cod liver oil
176	W. H. 4	14	6,407	Nonhomogeneous	0.195	0.130	66.7	5.3	0.045	Top milk formula. Cod liver oil. Very high calories per kilogram
19	G. H.	7.5	5,660	Constipated	0.193	0.060	46.8	9.5	0.023	Recovering from rickets. Cod liver oil just discontinued
119	W. H. 5	14	6,436	Nonhomogeneous	0.191	0.115	60.5	3.9	0.049	
101	J. K. 2	10	4,790	Softnormal	0.180	0.083	45.9	3.5	0.062	Underfed
67	W. R.	6	6,529	Constipated	0.159	0.012	23.6	3.1	0.033	15 c.c. milk of magnesia
81	A. B.	13	5,075	Normal	0.157	0.097	54.0	3.4	0.062	High proportion carbohydrate in diet
66	P. S. 3	10	6,440	Softnormal	0.167	0.064	38.2	3.6	0.046	Very low calories per kilogram
66	R. L. 1	12	10,160	Normal	0.152	0.069	45.3	2.9	0.053	Sweetened condensed milk. Very high proportion carbohydrate
66	L. B.	3.5	3,336	Nonhomogeneous	0.148	0.051	34.6	3.5	0.047	Very low calories per kilogram
53	A. F.	6	6,540	Softnormal	0.136	0.079	51.7	2.3	0.060	Top milk formula. Low calories per kilogram
60	R. P.	10	9,514	Normal	0.088	0.014	15.2	3.8	0.043	Much underfed. Rather high proportion carbohydrate in diet
65	M. M.	11	11,160	Normal	0.087	0.013	16.0	2.1	0.043	Malted milk. Extremely high proportion carbohydrate in diet
94	J. W.	3	3,676	Softnormal	0.069	0.014	0.6	0.9	0.057	

By calcium *absorption* is here meant the difference between the calcium intake and the excretion of calcium in the stools.

The values for ash and calcium in the feces were obtained by analysis of the dried material. The ash was determined by the Stölte method,¹ which consists of the application of heat to the finely ground material in a platinum dish inside a porcelain or silica dish, without the addition of acid or alkali. The calcium was determined in the weighed ash by the McCrudden method.²

In some of the cases, especially when the children were taking a mixed diet, the calcium in the food was not determined by direct analysis, but was estimated from the known weight or measurement of the various articles of the food intake. The calcium content of some of the articles of food which made up the diet had previously been determined in this laboratory.

In this article are presented only the findings for infants taking modifications of cow's milk. The data for children taking mixed diet will be discussed in a later paper.

HEALTHY INFANTS

The first group of infants here considered were normal or approximately normal as to their digestion. Most of these children were healthy and gaining weight at the time of observation. None of them had diarrheal stools. Table 1 shows the relation of the calcium absorption to the calcium and the fat intake for the group. These values are expressed as grams per kilogram of body weight. Only in this way could the intake for infants of widely differing weights be correlated. A study of the values for total intake and absorption of calcium, weight not being considered, showed no consistent variation in absorption as related to intake.

Calcium Absorption and Its Relation to Calcium Intake.—The intake of calcium oxid per kilogram ranged from 0.13 to 0.30 gm., with an average of 0.22 gm. in twenty-six of the thirty cases studied. Of the remaining four cases, in one the intake of calcium oxid was extremely high, and in the others it was very low. In twenty instances the intake of calcium oxid was more than 0.19 gm.

The relation of the calcium absorption to the calcium intake is summarized in Table 2. It is here seen that the best absorption occurred when the intake exceeded 0.19 gm. per kilogram, and that when the intake was less than 0.10 gm. the absorption was very poor.

1. Stölte: *Biochem. Ztschr.* **35**:104, 1911.

2. McCrudden: *J. Biol. Chem.* **10**:187, 1911.

In the one case with exceptionally high intake, the absorption was only 0.099 gm. per kilogram, which was lower than in many cases where the intake was less.

The average absorption of calcium oxid in all the cases in which the intake exceeded 0.10 gm. per kilogram, was 0.089 gm. per kilogram. This value is higher than that found for breast fed infants. With five breast fed infants, having an intake of calcium oxid ranging from 0.045 to 0.097 gm. per kilogram and averaging 0.081 gm., we found an absorption of from 0.035 to 0.071 gm. per kilogram averaging 0.054 gm. In the much quoted case reported by Blauber³ the intake of calcium oxid was 0.041 gm. per kilogram and the absorption was 0.031 gm. per kilogram.

TABLE 2.—RELATION OF CALCIUM ABSORPTION TO CALCIUM INTAKE

CaO Intake per Kg.	No. of Cases	Absorption of CaO Over 0.09 Gm. per Kg.	Absorption of CaO, 0.06 to 0.09 Gm. per Kg.	Absorption of CaO Under 0.06 Gm. per Kg.
Over 0.19 gm.	20	15	3	2
Under 0.19 gm.	10	1	4	5
Under 0.10 gm.	3	0	0	3

Relation of Calcium Absorption to Fat Intake.—In twelve of the sixteen cases in Table 1 in which the absorption of calcium oxid exceeded 0.09 gm. per kilogram, the intake of fat exceeded 4.2 gm. per kilogram. In the other four cases in which the absorption of calcium oxid exceeded 0.09 gm. per kilogram the fat intake was less than 4.2 gm. per kilogram, but other factors were present which may have influenced the calcium absorption. One child had been receiving cod liver oil up to the time of the observation; another child had received one-half ounce of milk of magnesia; the other two children were taking a dried milk formula, in which the calcium may be present in a more easily assimilated form as a result of the treatment to which the milk has been subjected during the process of drying. In only four of the fourteen cases in which the absorption of calcium oxid was less than 0.09 gm. per kilogram was the fat intake as great as 4.2 gm. per kilogram.

In two-thirds of the cases in the table the food contained from 0.045 to 0.060 gm. of calcium oxid for every gram of fat. When the calcium oxid per gram of fat in the intake was less than 0.045 gm. per kilogram, the only high absorption of calcium oxid occurred when cod liver oil was being taken. This optimum ratio of fat and calcium intake existed in some cases when the intake of both calcium and fat was too low. It has been noted that the best calcium absorption took

3. Blauber³: Ztschr. f. Biol. 40:36, 1900.

place when the intake of fat was 4.2 gm. or more per kilogram. The lowest value for calcium oxid intake per kilogram which would maintain the optimum ratio of calcium oxid to this amount of fat in the intake therefore would be 0.19 gm. per kilogram, a value already noted as the amount necessary to secure good absorption.

Percentage Absorption of Calcium.—From 35 to 55 per cent. of the calcium intake was absorbed in eighteen of the thirty cases. The only higher values for percentage absorption were noted twice with a child who was recovering from rickets and who had been receiving cod liver oil for a long period. A higher percentage of the calcium intake is absorbed by breast fed infants. In our cases the average for breast fed infants was 66.7 per cent.; in Blauberger's case the absorption was 75.6 per cent.

Calcium Requirement.—The average absorption of calcium oxid found for five breast fed infants was 0.054 gm. per kilogram. Since, according to our observations, infants taking modifications of cow's milk absorbed on the average only about 45 per cent. of the calcium intake, it is necessary to provide for them a minimum intake of about 0.130 gm. of calcium oxid per kilogram to insure even the low average absorption of breast fed infants; there would, therefore, seem to be danger in an intake lower than this. On the other hand, there appears to be no advantage in an intake greater than 0.30 gm. per kilogram. Hoobler⁴ says that anything less than 1.0 or 1.5 gm. of calcium oxid daily should be considered a calcium poor intake for infants taking modifications of cow's milk. His requirement, calculated for an infant of seven kilograms body weight, would be from 0.143 to 0.215 gm. of calcium oxid per kilogram of body weight. This range includes our above noted value, 0.19 gm., the intake of calcium oxid per kilogram found to be necessary to secure good absorption.

Other Factors in Relation to Calcium Absorption.—The values presented in Table 1 show that there was no definite variation in calcium absorption per kilogram according to the age or weight of the child.

There was also no definite relation between the type of stool and the amount of calcium oxid absorbed per kilogram or the percentage of the calcium intake absorbed.

Table 3 shows for the cases considered in Table 1 the calcium excretion in the stools in relation to the actual calcium and the fat intake; also the relation of the calcium excretion to the excretion of fat and of soap in the stools.

Calcium Excretion and Its Relation to Calcium Intake and to Fat Intake.—With the exception of two unusually high values the excre-

4. Hoobler: Am. J. Dis. Child. 2:107, 1911.

tion of calcium in the stools ranged from 0.34 to 1.06 gm., with an average of 0.70 gm. As a rule, the higher the calcium intake the higher the calcium excretion; the lower the intake, the lower the excretion. In general, the fat intake and the calcium intake were parallel, so that a high calcium excretion occurring with a high fat intake could be accounted for by a high calcium intake. When a high fat intake accompanied a low calcium intake, the excretion of calcium was low, except in one case. Hence, there is little evidence that there is any constant relation between the amount of the fat intake and the amount of calcium excreted in the stools.

TABLE 3.—CALCIUM EXCRETION OF HEALTHY INFANTS IN RELATION TO ACTUAL CALCIUM AND FAT INTAKE

No.	Case	Stools	CaO In- take, Gm. Daily	Fat In- take, Gm. Daily	CaO in Stools, Gm. Daily	Fat in Stools, Gm. Daily	Fat as Soap in Stools, Gm. Daily	CaO Possibly Held as Soap, Percentage of	CaO in Stools	CaO In- take
113	J. S. 1	Nonhomogeneous	1.98	26.6	1.58	1.53	0.26	1.6	1.3	
158	H. B.	Normal	1.81	34.7	1.54	4.93	3.00	25.3	21.2	
71	P. D. 2	Constipated	1.20	22.6	1.06	3.34	2.64	24.9	22.0	
65	P. D. 3	Constipated	1.39	24.0	1.06	2.95	2.05	19.3	14.7	
54	R. C.	Normal	1.78	32.8	1.00	2.70	1.97	19.7	11.1	
67	M. R.	Constipated	1.23	23.4	0.94	2.79	2.25	24.0	18.3	
62	J. M.	Normal	1.20	24.4	0.89	1.14	1.01	11.4	9.6	
57	M. S. 2	Normal	1.63	29.4	0.87	3.36	2.42	27.8	14.9	
96	R. L. 1	Normal	1.58	30.0	0.86	2.04	1.47	17.0	9.3	
58	J. I.	Normal	1.56	28.6	0.81	1.30	1.11	13.2	7.1	
68	M. M.	Normal	1.00	23.3	0.81	1.24	0.96	11.5	9.6	
70	P. D. 1	Constipated	1.22	22.9	0.78	2.21	1.67	22.3	13.7	
63	F. N. 2	Softnormal	1.29	24.1	0.75	5.09	3.68	49.1	28.6	
81	R. B.	Normal	1.60	31.0	0.72	3.91	3.48	18.3	21.7	
50	B. P.	Normal	0.84	36.5	0.71	2.91	2.01	29.2	21.7	
82	P. L.	Nonhomogeneous	1.19	15.7	0.69	1.73	1.12*	16.3*	9.4*	
66	P. S. 3	Softnormal	1.10	23.7	0.68	0.85	0.30	4.4	2.7	
97	B. W. 1	Softnormal	1.36	27.6	0.67	2.54	1.81	27.6	13.3	
60	F. N. 1	Constipated	1.22	26.2	0.67	4.12	3.31	49.4	27.1	
86	J. M.	Softnormal	1.02	13.4	0.66	2.08	1.67	25.3	16.4	
72	A. K.	Constipated	1.16	22.1	0.64	3.04	2.22	31.7	19.1	
49	G. H.	Constipated	1.09	18.3	0.58	2.98	2.33	19.2	21.4	
166	A. A.	Nonhomogeneous	0.78	11.4	0.56	2.16	0.01	0.7	0.1	
94	E. W.	Softnormal	0.26	3.4	0.50	1.00	0.75	15.0	29.0	
119	W. H. 5	Nonhomogeneous	1.24	25.2	0.49	2.64	0.78*	15.9*	6.3*	
101	J. K. 2	Softnormal	0.85	16.5	0.46	0.66	0.16	10.0	5.4	
83	A. P.	Softnormal	0.89	15.1	0.43	0.65	0.50	11.6	5.6	
126	W. H. 4	Nonhomogeneous	1.26	35.8	0.42	3.35	1.09*	10.2*	13.4*	
85	C. M.	Nonhomogeneous	0.79	11.4	0.39	1.64	1.05*	26.9*	18.4*	
92	L. B.	Nonhomogeneous	0.52	12.5	0.31	2.06	1.28*	10.7*	20.6*	

* Value possibly too high. Stools acid.

Relation of Calcium Excretion to Excretion of Total Fat and of Fat as Soap.—There was no constant relation between the excretion of total fat and the excretion of calcium in the stools. In order to study the relation between the excretion of calcium and that of fat as soap, the findings shown in Table 2 were averaged by groups according to the type of stool, since the average soap excretion varies definitely with the type of stool. These averages (Table 4) show that the cal

cium excretion was more closely related to the calcium intake than it was to the excretion of soap. In the constipated stools there was a greater soap content than in the normal stools, but a smaller content of calcium, corresponding to a smaller calcium intake. The group of softnormal stools had a much greater soap content than that of the nonhomogeneous stools, but here, again, a somewhat lower calcium content corresponded to a somewhat lower calcium intake.

TABLE 4.—RELATION OF AVERAGE CALCIUM EXCRETION TO THE AVERAGE SOAP EXCRETION

Stools	No. of Cases	CaO Intake, Gm. Daily	CaO in Stools, Gm. Daily	Fat as Soap in Stools, Gm. Daily	CaO Possibly Held as Soap	CaO not Held as Soap	CaO Possibly Held as Soap, Percentage of	
							CaO In Stools	CaO Intake
Constipated.....	7	1.22	0.82	2.35	0.24	0.58	30.9	19.5
Normal.....	9	1.45	0.92	2.04	0.20	0.72	22.6	14.4
Softnormal.....	7	0.97	0.59	1.31	0.13	0.46	20.4	14.4
Nonhomogeneous.....	7	1.11	0.64	0.90	0.09	0.59	20.3	10.1

There is a prevalent opinion that in soapy stools an excessive loss of calcium occurs, which may take place either as calcium bound to the fat in the form of insoluble soaps or as calcium phosphate. To show to what extent calcium was lost as insoluble soaps, values have been included in Table 3 giving the percentage of the total calcium *excretion* which could possibly be held in the form of soap, and also the percentage of the calcium *intake* which could be lost in this way. The amount of calcium that could be bound as soap is approximately one-tenth the amount of soap in the stool, since the combining ratio of calcium to the higher fatty acids is about one to ten. (Combining weight of calcium oxid is 28; stearic acid, 284.) The calcium bound as soap was never found to be as much as five-tenths and seldom more than three-tenths of the total calcium excretion. In all the cases in which the calcium lost as soap was more than three-tenths of the total calcium excretion the *total* loss of calcium was not excessive. In no case was the calcium lost as soap equal to three-tenths of the calcium *intake*.

The average values according to type of stool, included in Table 4, show that when the stools were constipated a greater proportion of both the calcium excretion and the calcium intake was lost as soap, but that the total loss of calcium and also the calcium intake averaged distinctly less for this group than for the group of normal stools.

Table 4 also includes average values to show to what extent calcium could be lost as phosphate in the different types of stools. These values were obtained by subtracting from the average total calcium excretion the amount of calcium which could be held as soap, that is,

one-tenth of the value for soap excretion. The remaining amount of calcium in the stools is the maximum that could be held as phosphate. Thus, it is shown that the amount of calcium that could be held as phosphate was greatest in the group of normal stools, which had lower soap content than did the constipated stools. In fact, the average value for the calcium not held as soap for the group of constipated stools with the highest soap content was practically the same as that for the group of nonhomogeneous stools with the lowest soap content. These observations seem to establish quite definitely that in soapy stools there is not an increased excretion of calcium phosphate. The excretion of calcium not held as soap was influenced more by the amount of calcium intake than by any other factor.

RACHITIC INFANTS

The second group of infants considered were suffering from rickets. Several of them also had tetany, either mild or severe. None of these children had diarrheal stools. Table 5 shows the absorption of calcium per kilogram and its relation to the calcium and the fat intake.

Calcium Absorption.—The intake of calcium oxid per kilogram of body weight was, in general, lower and the range was narrower than was the case with normal infants. In the majority of the cases the intake was less than 0.19 gm. per kilogram, which we have noted as the minimum to insure good absorption by healthy infants. The absorption of calcium oxid per kilogram by the rachitic infants as a group was extremely poor. In only one observation was there good absorption, that is, more than 0.09 gm., the average found for normal infants. In only six of the twenty-three observations was the absorption as much as 0.06 gm. per kilogram. In the cases where there was fair absorption of calcium oxid, the children either had been taking cod liver oil or were at the time suffering from severe tetany. In the one instance in which the absorption was high the child had been receiving cod liver oil for two and one-half months. The two next highest values were found with a child who had been taking cod liver oil for about one week. In these three instances the fat intake per kilogram was the highest shown in the table and was accompanied by a high intake of calcium oxid. Although several children showing a very low absorption were at the time of observation taking cod liver oil, none had received it for more than a few days. Of five observations on children suffering from tetany with convulsions, in only one instance was the absorption of calcium oxid less than 0.05 gm. per kilogram, which is a value higher than the average for rachitic infants.

The average absorption for the group of rachitic infants was 0.042 gm. per kilogram, which is less than one half that found for the normal infants.

TABLE 5.—ABSORPTION OF CALCIUM BY RACHITIC INFANTS

No.	Case	Age in Mos.	Weight in Gm.	Stools	Intake of CaO Gm. per Kg.	CaO Absorbed Gm. per Kg.	Per Cent. Intake absorbed	Intake of Fat Gm. per Kg.	Grams of CaO Intake per Fat Intake	Remarks
390	J. D. 4	5	3,901	Softnormal	0.249	0.077	30.9	6.7	0.037	Mild tetany. Cod liver oil for about one week
401	E. C. 1	11	6,724	Nonhomogeneous	0.247	-0.013	0.0	5.0	0.049	
64	L. R. 2	12	3,883	Softnormal	0.242	0.136	56.2	6.3	0.038	Cod liver oil
402	L. R. 1	9.5	3,454	Loose	0.240	0.055	22.9	4.6	0.053	
388	J. D. 1	5	3,845	Loose	0.235	0.065	27.6	3.9	0.040	Tetany. One very severe glottis spasm
389	J. D. 3	5	3,976	Loose	0.238	0.084	36.8	5.1	0.045	Cod liver oil for few days before observation
397	L. E.	8.5	7,305	Nonhomogeneous	0.210	0.029	13.8	4.7	0.045	Mild tetany, marked rickets.
61	P. C. 2	14	7,789	Constipated	0.193	0.032	16.6	3.3	0.059	Rather high proportion carbohydrate in diet
400	H. S.	9	7,825	Nonhomogeneous	0.184	0.049	26.6	2.5	0.073	Protein milk. Recently changed from breast. Severe tetany
394	J. T. 1	9	6,734	Constipated	0.183	0.012	6.6	3.7	0.049	
74	E. C. 3	15	7,788	Softnormal	0.181	-0.008	0.0	2.6	0.067	Rather low calories per kilogram
395	J. T. 2	9	6,827	Constipated	0.177	0.036	20.3	3.7	0.048	Injection saline first day
398	B. M. 1	7	5,646	Nonhomogeneous	0.165	0.063	38.1	3.8	0.044	Mild rickets, tetany
391	P. L. 1	10	9,612	Constipated	0.158	0.055	34.7	3.3	0.048	Recently changed from breast milk. High carbohydrate. Mild rickets
393	P. L. 3	10	9,560	Normal	0.153	0.019	12.4	3.2	0.049	High carbohydrate. Mild rickets
387	D. W. 3	5	5,733	Nonhomogeneous	0.153	0.038	24.8	4.0	0.038	Cod liver oil. Magnesium sulphate injection. Convulsions
392	P. L. 2	10	9,574	Constipated	0.152	0.057	37.5	3.2	0.048	Mild rickets. Injection of magnesium sulphate
386	D. W. 1	5	5,815	Nonhomogeneous	0.148	0.055	37.2	3.1	0.048	Prompt and severe convulsions. Recently changed from breast milk
155	D. W. 2	5	5,816	Nonhomogeneous	0.145	0.065	44.8	3.0	0.049	Low calories per kilogram. Tetany with convulsions
154	W. H. 1	12	7,048	Nonhomogeneous	0.133	-0.017	0.0	2.5	0.054	Rather low calories per kilogram
289	T. W.	9	5,144	Nonhomogeneous	0.134	0.020	16.1	2.4	0.051	Mild tetany
117	W. H. 2	12	7,140	Normal	0.117	0.020	17.1	3.6	0.033	Cod liver oil for two days before observation. Low calories per kilogram
396	G. S.	9.5	7,445	Nonhomogeneous	0.073	0.033	45.2	3.0	0.024	Recently changed from breast milk. Cod liver oil. Marked rickets. Mild tetany

The poor absorption of calcium in rickets is strikingly shown by the values for percentage absorption. In fifteen of the twenty-three cases the percentage absorption was lower than the usual range for normal children.

The intake of fat per kilogram as well as that of calcium per kilogram was, on the whole, lower with the rachitic than with the normal children. The relation of the calcium intake to the fat intake was in most cases similar to that of the normal group.

TABLE 6.—CALCIUM EXCRETION BY RACHITIC INFANTS

No.	Case	Stools	CaO	Fat	CaO	Fat	Fat	CaO Possibly
			Intake, Gm. Daily	Intake, Gm. Daily	Intake, Gm. Daily	Intake, Gm. Daily	Intake, Gm. Daily	Held as Soap, Percentage of
401	E. C. 1	Nonhomogeneous	1.66	33.9	1.75
74	E. C. 3	Softnormal	1.41	21.1	1.47	2.71	1.76	12.0
397	L. E.	Nonhomogeneous	1.56	34.9	1.34
393	P. L. 3	Normal	1.46	30.1	1.28
61	E. C. 2	Constipated	1.50	25.5	1.25	1.71	1.12	9.0
394	J. T. 1	Constipated	1.23	27.1	1.16	7.5
154	W. H. 1	Nonhomogeneous	0.94	17.4	1.06	0.91	0.49	4.7
391	P. L. 1	Constipated	1.52	31.4	0.99	5.2
395	J. T. 2	Constipated	1.21	25.0	0.97
400	H. S.	Nonhomogeneous	1.44	19.7	0.03
392	P. L. 2	Constipated	1.46	30.2	0.91
117	W. H. 2	Normal	0.84	25.4	0.69	2.24
390	J. D. 4	Softnormal	0.97	26.2	0.67
388	J. D. 1	Loose	0.90	15.1	0.66
387	D. W. 3	Nonhomogeneous	0.88	23.0	0.66
402	L. R. 1	Loose	0.83	15.7	0.64
389	J. D. 3	Loose	0.90	20.1	0.57
398	B. M. 1	Nonhomogeneous	0.93	21.1	0.57
386	D. W. 1	Nonhomogeneous	0.86	17.9	0.54
399	T. W.	Nonhomogeneous	0.64	12.6	0.53
155	D. W. 2	Nonhomogeneous	0.84	17.2	0.46	3.73	2.06*	11.7*
64	L. R. 2	Softnormal	0.94	24.6	0.41	3.00	1.21*	29.5*
390	G. S.	Nonhomogeneous	0.55	22.6	0.30	12.9*

* Value possibly too high. Stools acid.

Table 6 gives for the rachitic children the calcium excretion in the stools together with the calcium and the fat intake. In the few cases in which fat values in the stools were obtained, there is shown the relation of the calcium excretion to that of total fat and fat as soap.

Calcium Excretion.—The range in calcium excretion was wider with rachitic than with normal children. There were seven values exceeding 1.0 gm. and the average, 0.86 gm., was higher than the normal average, 0.70 gm. In general, the excretion of calcium was related to the calcium intake, but not to the fat intake. In the few cases in which fat determinations in the stools were made the calcium excretion was found to be entirely unrelated to the amount of either total fat or fat as soap in the stools. In two instances there was a very large fat excretion in the stools and a very small calcium excretion; in three others there was a high calcium excretion, but only a small part of this excretion was in the form of soap.

TABLE 7.—ABSORPTION OF CALCIUM BY INFANTS SUFFERING FROM DIARRHEA

No.	Case	Age in Mos.	Weight in Gm.	Stools	Intake of CaO Gm. per Kg.	CaO Absorbed Gm. per Kg.	Per Cent. Intake Absorbed	Intake of Fat, Kg.	Grams of CaO Intake per Gm. Fat	Remarks
135	F. H. 4	11	4,838	Diarrheal	0.412	0.113	27.6	4.1	0.100	Evaporated milk formula. Very large fermentative stools
139	S. J.	9	4,922	Severely diarrheal	0.302	0.063	17.4	5.9	0.061	
132	F. H. 1	10	4,442	Severely diarrheal	0.318	0.059	16.9	7.3	0.048	Evaporated milk formula. Very large fermentative stools
136	F. H. 2	10	4,040	Diarrheal	0.332	0.043	13.0	7.2	0.046	
175	I. G.	2.5	2,930	Diarrheal	0.304	0.021	6.7	5.0	0.061	
106	V. C. 3	5	4,419	Diarrheal	0.382	0.138	42.2	6.8	0.041	Tetany, rickets, taking cod liver oil
121	V. C. 2	5	4,575	Severely diarrheal	0.248	0.069	23.9	5.2	0.048	
120	V. C. 1	5	4,566	Severely diarrheal	0.234	0.062	26.6	5.1	0.048	
143	F. S.	6	4,147	Mildly diarrheal	0.233	0.000	0.0	4.5	0.052	
139	J. D. 2	5	3,930	Diarrheal	0.217	0.038	17.7	4.4	0.050	
152	M. R.	4	3,001	Diarrheal	0.170	0.023	13.7	1.8	0.065	High proportion carbohydrate in diet Recently changed from breast milk
144	V. R. 2	3	6,357	Mildly diarrheal	0.154	0.038	24.5	2.9	0.052	
127	J. W. 4	6	5,724	Diarrheal	0.147	0.053	35.7	3.9	0.038	
123	E. R. 3	11	7,367	Diarrheal	0.136	0.058	43.0	3.2	0.043	Rickets, tetany, taking cod liver oil. Low calories per kilogram
147	W. H. 3	14	6,734	Diarrheal	0.134	0.071	53.3	2.7	0.049	
111	E. R. 2	10	7,436	Diarrheal	0.128	0.030	23.2	3.6	0.035	Rickets, tetany, taking cod liver oil. Low calories per kilogram
131	E. R. 1	10	7,540	Diarrheal	0.123	0.000	0.0	2.2	0.055	
161	B. S. 1	12	8,105	Diarrheal	0.107	0.010	8.3	1.9	0.063	Rickets, tetany. Rather high carbohydrate in diet. Excessively large stool
176	B. S. 2	13	7,708	Severely diarrheal	0.095	0.004	4.1	1.5	0.063	

INFANTS SUFFERING FROM DIARRHEA

The third group of infants considered were suffering from diarrhea. Some of them were also rachitic, but are placed in this group because the diarrheal condition is the chief factor in determining the composition of the stools. Table 7 gives the absorption of calcium oxid per kilogram and its relation to the calcium and fat intake for these infants.

Calcium Absorption.—The range in intake of calcium per kilogram was very wide, and there were more high values than were found with normal infants. This was due largely to the fact that these infants were much under size. The absorption of calcium oxid was generally low. Only five of the nineteen values exceeded 0.06 gm. per kilogram; only two exceeded 0.09 gm. per kilogram. One of these two children had been receiving cod liver oil for about one week, and the other had a very high intake of calcium. The third highest absorption was in the case of a child who had been receiving cod liver oil just before the period of observation.

The average absorption for this group of infants was 0.046 gm. of calcium per kilogram, about one half that found for normal children.

The percentage absorption was also much below normal. Only four of the nineteen values fell within the normal range.

The fat intake per kilogram varied widely and bore no constant relation to the calcium absorption. Successive observations on two children, V. C. and E. R., showed that the calcium absorption increased as the diarrhea improved. Both these children were taking cod liver oil.

TABLE 8.—CALCIUM EXCRETION BY INFANTS SUFFERING FROM DIARRHEA

No.	Case	Stools	CaO In- take, Gm. Daily	Fat In- take, Gm. Daily	CaO In Stools, Gm. Daily	Fat In Stools, Gm. Daily	Fat as Soap in Stools, Gm. Daily	CaO Possibly Held as Soap, Percentage of	
								CaO in Stools	CaO In- take
100	S. J.	Severely diarrheal	1.78	29.1	1.47	14.54	1.29*	8.8*	7.3*
135	F. H. 4	Diarrheal	1.99	20.0	1.44	1.77	0.22*	1.7*	1.1*
136	F. H. 2	Diarrheal	1.54	33.6	1.34	4.61	0.87*	6.7*	5.6*
132	F. H. 1	Severely diarrheal	1.51	32.4	1.28	6.91	1.06*	8.3*	6.9*
143	F. S.	Mildly diarrheal	0.97	18.7	0.98	4.20	1.19*	12.2*	12.3*
131	E. R. 1	Diarrheal	0.93	16.8	0.94	3.35	0.00	0.0	0.0
164	B. S. 1	Diarrheal	0.97	13.5	0.89	3.07	0.00	0.0	0.0
121	V. C. 2	Severely diarrheal	1.13	23.6	0.86	10.38	0.34*	4.0*	3.0*
175	I. G.	Diarrheal	0.89	14.7	0.83	11.62	0.86*	10.4*	9.7*
120	V. O. 1	Severely diarrheal	1.09	23.6	0.80	5.77	0.00	0.0	0.0
144	V. R. 2	Mildly diarrheal	0.98	18.7	0.74	1.88	0.58*	7.8*	5.9*
111	E. R. 2	Diarrheal	0.95	27.1	0.73	3.76	0.00	0.0	0.0
139	J. D. 2	Diarrheal	0.85	17.0	0.70	6.01	0.82*	11.7*	9.7*
176	B. S. 2	Severely diarrheal	0.73	11.6	0.70	10.08	0.00	0.0	0.0
106	V. C. 3	Diarrheal	1.24	30.2	0.63	6.73	0.00	0.0	0.0
123	E. R. 3	Diarrheal	1.00	23.4	0.57	4.97	0.00	0.0	0.0
127	D. W. 4	Diarrheal	0.84	22.2	0.54	5.38	0.83*	15.2*	9.8*
152	M. R.	Diarrheal	0.51	5.4	0.41	3.61	0.13*	2.8*	2.6*
147	W. H. 3	Diarrheal	0.60	18.4	0.42	2.10	0.57*	13.7*	6.4*

* Value possibly too high. Stools acid.

Table 8 shows the calcium excretion and its relation to the calcium and the fat intake and to the excretion of total fat and of fat as soap in the stools of infants with diarrhea.

Calcium Excretion.—Both the calcium excretion and the calcium intake showed a wide range. The higher excretion usually occurred with the higher intake. The average excretion of calcium oxid was 0.86 gm. As in the other groups there was no definite relation between the fat intake and the calcium excretion. In some instances when the fat intake was high the calcium intake was also high, and the excretion of calcium higher than when the intake of calcium was lower. In this group, as in the others studied, there was no relation between the calcium excretion and the total fat excretion in the stools. Since the excretion of fat as soap in these acid stools was very low, evidently there was no relation between the excretion of calcium and that of fat as soap.

TABLE 9.—AVERAGE PROPORTIONS OF CALCIUM AND OF SOAP IN STOOLS OF INFANTS

Condition of Infants	Food	Stools	No. of Cases	CaO Intake, Gm. Daily	CaO, Per-centage of Total Solids	CaO, Per-centage of Total Solids	Fat as Soap, Per-centage of Total Solids
Normal	Cow's milk	Constipated	13	1.21	11.1	49.6	30.0
Normal	Cow's milk	Normal	19	1.23	11.8	47.5	24.5
Nearly normal	Cow's milk	Softnormal	7	1.06	10.0	46.3	17.7
Mostly delicate	Cow's milk	Nonhomogeneous	13	1.02	7.9	40.9	13.6*
Sick	Cow's milk	Diarrheal	13	1.05	6.3	32.5	2.8*
Sick	Cow's milk	Severely diarrheal	6	1.12	4.4	25.2	2.8*
Rachitic	Cow's milk	Constipated or normal	9	1.37	12.7	44.7	15.7†
Rachitic	Cow's milk	Softnormal or non-homogenous	14	0.94	8.1	39.1	15.5‡
Normal	Breast milk	Normal	3	(0.38)§	3.4	37.4	23.4*
Normal	Breast milk	Nearly normal, partly green	12	(0.38)§	4.3	42.9	12.0*
Normal	Breast milk	Green, with mucus	5	(0.38)§	3.0	39.6	4.2*
Sick	Breast milk	Diarrheal	4	0.22	1.8	18.4	4.6*
M. 1, normal	Top milk.	Normal	1	0.27	2.1	28.0	50.6
2. W., normal	cream dilution						
	Malted milk	Softnormal	1	0.26	7.5	40.6	11.0

* Value possibly too high. Stools acid.

† Only two values included in this average.

‡ Only three values included in this average.

§ Average of five values for normal children.

PROPORTION OF CALCIUM AND OF SOAP IN THE STOOLS OF INFANTS

Table 9 gives the average proportion of calcium in various types of stools of infants and its relation to the other constituents of the stools and to the calcium intake. There are given values not only for stools of infants taking modifications of cow's milk, but also for a number of stools of breast fed infants.

The stools of infants taking modifications of cow's milk which contained the smallest proportion of water, that is, the constipated and the normal stools, showed on the average the higher calcium percentage of total solids. With increased proportion of water the calcium percentage of total solids became less. The total calcium excretion was not thereby diminished, however, but rather increased, since the daily amount of total solids was greatly increased with the higher water content. The calcium percentage of total solids appeared to be more closely related to the looseness of the stools than to the amount of calcium intake, since there was but little variation in average intake for the different groups.

The calcium percentage of total solids of the constipated or normal stools of rachitic infants was higher than that of the corresponding type of stools of normal infants. It is not evident whether this increased percentage was due to the condition of rickets or to the higher average intake.

The average values for calcium percentage of total *salts* also were less as the stools became more watery. In other words, the proportion of salts not calcium, that is, the soluble salts, increased with the water content of the stools.

In stools of rachitic infants, although the total salts were increased over the normal, the calcium formed a smaller percentage of the total salts than in the corresponding stools of normal children. This shows that the other salts were increased more than was the calcium.

The proportion of the total solids which was soap in the stools of infants taking modifications of cow's milk was closely related to the water content, diminishing strikingly as the water in the stools increased. In the looser types of stools the decrease in soap percentage with increase in water content was accompanied by a similar though less marked decrease in the proportion of calcium. This association was not found in the constipated and the normal stools. The normal stools showed a lower proportion of fat as soap, with a slightly higher percentage of calcium, than did the constipated stools.

An entirely different range of values was seen with breast fed infants. With a much lower intake of calcium, the calcium percentage of total solids in the stools was much lower than when the food was modifications of cow's milk. The diarrheal stools of breast fed infants showed a much lower calcium percentage of both total solids and total salts than did the other types of stools. The other groups of the stools of breast fed infants did not differ much from one another in water content and varied little in the calcium percentage of total solids or of total salts. The calcium formed a somewhat smaller part of the total salts than in the stools of artificially fed infants.

The fat as soap, as well as the calcium oxid, formed a smaller proportion of the total solids in the stools of breast fed infants than in those of infants taking cow's milk, and was less in the diarrheal than in the normal stools. In the three groups of stools of breast fed infants which were normal as to water content, the proportion of soap was lower the less normal the appearance of the stool, while the calcium percentage of total solids varied but little.

The proportion of calcium in the stools in two instances of unusual feeding, with extremely low calcium intake, are included in Table 9. In the first instance, in which the food was a cream dilution, the calcium percentage of both total solids and total salts was very low, even lower than that found with breast fed infants. This stool had a very high percentage of soap, due to the administration of a large amount of milk of magnesium. In the other instance, in which the child received malted milk, the calcium percentage of total solids and of total salts was somewhat lower than that found for the same type of stool when the food was a modification of cow's milk.

The following summary gives answers, based on our observations, to such of the questions stated in the introduction as apply to infants taking modifications of cow's milk.

SUMMARY

1. The average absorption of calcium oxid by healthy infants taking modifications of cow's milk was 0.09 gm. per kilogram of body weight. Since the average absorption of calcium oxid by breast fed infants was about 0.6 gm. per kilogram, it may be assumed that 0.06 gm. per kilogram is the minimum normal absorption by infants taking modifications of cow's milk.

The daily total excretion of calcium oxid in the stools ranged from 0.34 to 1.06 gm., averaging 0.70 gm.

2. The excretion and the absorption of calcium were, in general, dependent on the amount of calcium intake, from 35 to 55 per cent. of the intake being absorbed.

To insure the average absorption of 0.09 gm. of calcium oxid per kilogram, the intake of calcium oxid should be at least 0.19 gm. per kilogram; to insure an absorption equal to the average found for breast fed infants the intake of calcium oxid should be at least 0.13 gm. per kilogram.

The best absorption of calcium was obtained when the calcium intake bore a definite relation to the fat intake, that is, when the food contained from 0.045 to 0.060 gm. of calcium oxid for every gram of fat and when at the same time the fat intake was ample, not less than 4.0 gm. per kilogram.

3. An excessive calcium intake apparently did not increase the calcium absorption, the excess being excreted. When the intake of calcium oxid was very low, less than 0.10 gm. per kilogram, the absorption of calcium oxid was less than the normal calcium requirement of the body.

4. The *total* absorption of calcium oxid varied in general with the weight of the child; the *per kilogram* absorption did not vary regularly with either the age or the weight.

5. The relation of calcium excretion to soap excretion was not constant. The excretion of *soap* was directly related to the type of stool, that is, to the water content and to the reaction of the stool. The excretion of *calcium* was closely related to the calcium intake. On the average, the normal and the constipated stools, with high soap content, were found when the intake of calcium was high and, therefore, they showed the higher excretion of calcium. However, constipated stools, which contained more soap than normal stools, had lower calcium content. Nonhomogeneous stools, with the lowest average soap content, showed the same content of calcium not held as soap as did the constipated stools, with the highest soap content.

6. The calcium that could be lost as soap was never a large proportion of the calcium intake. Even in the stools containing the most soap it was found to be less than three-tenths the calcium intake. The calcium lost as phosphate was shown not to be increased in soapy stools.

7. The calcium percentage of the total solids varied, as a rule, with the water content of the stools, diminishing as the water increased.

8. The calcium absorption was much lower when diarrhea was present. With an increased excretion of calcium in diarrheal stools, there was a marked decrease in soap excretion.

The calcium absorption by rachitic infants was much lower than that by healthy infants.

In the few cases in which observations were made on infants recovering from rickets, the calcium absorption was higher than the normal average. These infants had received cod liver oil for a considerable period.

9. The administration of cod liver oil regularly increased the absorption of calcium, unless diarrhea was present.

INCIDENCE OF PROTEIN SENSITIZATION IN THE NORMAL CHILD

HORACE MITCHELL BAKER, M.D.
Alumni Research Fellow Children's Hospital
BOSTON

The object of this paper is to show the incidence of protein sensitization in the normal child. Subsequent papers will show the incidence of sensitization in asthmatic and eczematous patients in comparison with the normal.

This study of protein sensitization in its relationship to the diseases of infancy and childhood as manifested in eczema, asthma and urticaria, has been made possible through alumni of this institution.

This research has necessarily been brought to a standstill, before definite conclusions could be reached because of the war, but the results thus far are very suggestive and of interest to the pediatrician to note the striking difference between the incidence of sensitization in the normal as compared with the child showing anaphylactic symptoms.

Within a few years, numerous reports have appeared in regard to the treatment of hay-fever and asthmatic patients by determining the presence or absence of protein sensitization. In all of these reports there have unquestionably been sufficient controls to check the relationship, but it has seemed to me in studying the problem of protein sensitization, that it is highly important to have as control a series of tests in normal cases, which will determine (1) the incidence of sensitization in the normal child; (2) show the relative frequency of sensitization to the specific proteins; (3) give a standard by which results of the reactions on anaphylactic patients may be determined properly.

To carry out this test for the detection of hypersusceptibility toward various proteins, the preparation of extracts are of fundamental importance. In order to get the best results it is essential that the preparations used should readily be held in suspension. They should be sterile and suspended in a non-irritating and readily absorbable diluent.

In the preparation of the protein extracts, the first obvious step is to avoid the use of chemicals which may form insoluble compounds with the proteins present or form new compounds which might lead to erroneous results. Consequently, the proteins of vegetables and fruits have been prepared as described by Woodhouse. The methods principally used were described in a previous study by Baker and Floyd on protein extracts in states of hypersensitization.

All proteins employed in this study were used on anaphylactic as well as on normal patients, so that a comparison can be made between the patients giving no anaphylactic symptoms and those with varying degrees of sensitization.

(1) 1.

2.

3.

Types of reactions in skin sensitization test. 1. Control. 2. Moderate reaction. 3. Severe reaction.

The method employed to determine sensitization was carried out in the following manner: The inner side of the forearm was cleaned with alcohol and ether, scarifications or scratches were made about two inches apart, allowing the oozing of serum only. The upper scratch was kept for a control. One or two drops of the protein in normal saline or tenth normal sodium hydroxid are placed on the other scratches and allowed to be absorbed. Both points of inoculation are examined at five minute intervals for half an hour.

Positive reactions consist of a raised urticarial wheal, surrounded by an area of redness of the skin, irregular in outline and usually from 6 to 20 mm. in diameter. The reactions described as questionable consist either of a slight elevation about the point of inoculation or of a small area of erythema. Such reactions are considered negative for diagnostic purposes. They are noted and repeated at a later time in that they may be positive or entirely negative on the subsequent examination. Negative reactions are those which do not differ from the control.

The number of positive, doubtful and negative reactions with each protein is shown.

TABLE 1.—CASES GIVING NO HISTORY OF ANAPHYLAXIS TESTED FOR SENSITIZATION TO VEGETABLES

	Number Tested	Number Positive	Questionable Number	Number Negative
Bean.....	24	0	0	24
Beet.....	24	0	0	24
Cabbage.....	24	0	0	24
Cucumber.....	24	0	0	24
Lettuce.....	24	0	0	24
Tomato.....	24	0	1	23
Onion.....	24	1	0	23
Parsnip.....	24	0	0	24
Peas.....	24	0	0	24
Potato.....	24	1	0	23
Squash.....	24	0	1	23
Spinach.....	24	0	1	23
Turnip.....	24	0	0	24

TABLE 2.—CASES GIVING HISTORY OF ANAPHYLAXIS TESTED FOR SENSITIZATION TO VEGETABLES

	Number Tested	Number Positive	Questionable Number	Number Negative
Beet.....	4	0	0	4
Bean.....	30	1	1	28
Spinach.....	15	1	0	14
Cabbage.....	18	0	0	18
Tomato.....	12	0	0	12
Carrots.....	14	0	0	14
Cucumbers.....	16	0	0	16
Lettuce.....	16	1	0	15
Potato.....	34	1	0	33
Parsnip.....	23	1	0	22
Peas.....	20	0	0	20
Squash.....	26	2	0	24
Turnip.....	17	1	0	16
Onion.....	2	1	0	1

TABLE 3.—CASES GIVING NO HISTORY OF ANAPHYLAXIS TESTED FOR SENSITIZATION TO EGGS AND MILK

	Number Tested	Number Positive	Questionable Number	Number Negative
Egg white.....	25	1	0	24
Whole egg.....	25	0	0	25
Casein.....	25	0	0	25
Lactalbumin.....	25	0	0	25

TABLE 4.—CASES GIVING HISTORY OF ANAPHYLAXIS TESTED FOR SENSITIZATION TO EGGS AND MILK

	Number Tested	Number Positive	Questionable Number	Number Negative
Eggs.....	74	6	6	62
Casein.....	76	4	0	72
Lactalbumin.....	51	0	1	50

TABLE 5.—CASES GIVING NO HISTORY OF ANAPHYLAXIS TESTED FOR SENSITIZATION TO FISH

	Number Tested	Number Positive	Questionable Number	Number Negative
Clam.....	25	0	0	25
Codfish.....	25	0	2	23
Haddock.....	25	0	1	24
Lobster.....	25	0	1	24
Salmon.....	25	4	1	20
Oyster.....	25	0	0	25

TABLE 6.—CASES GIVING HISTORY OF ANAPHYLAXIS TESTED FOR SENSITIZATION TO FISH

	Number Tested	Number Positive	Questionable Number	Number Negative
Codfish.....	33	0	0	33
Haddock.....	30	0	3	27
Salmon.....	25	0	3	22
Lobster.....	32	0	1	31
Clam.....	30	0	0	30
Crab.....	23	0	0	23
Oyster.....	28	0	1	27

TABLE 7.—CASES GIVING NO HISTORY OF ANAPHYLAXIS TESTED FOR SENSITIZATION TO GRAINS

	Number Tested	Number Positive	Questionable Number	Number Negative
Buckwheat.....	25	0	2	23
Barley.....	25	0	0	25
Corn.....	25	1	0	24
Oats.....	25	0	0	25
Rice.....	25	0	0	25
Rye.....	25	1	0	24
Wheat.....	25	0	0	25

TABLE 8.—CASES GIVING HISTORY OF ANAPHYLAXIS TESTED FOR SENSITIZATION TO GRAINS

	Number Tested	Number Positive	Questionable Number	Number Negative
Wheat.....	48	1	2	45
Oats.....	69	9	4	59
Rye.....	37	0	3	34
Barley.....	35	0	3	32
Rice.....	65	4	3	58
Corn.....	40	2	3	35
Buckwheat.....	26	0	1	25

TABLE 9.—CASES GIVING NO HISTORY OF ANAPHYLAXIS TESTED FOR SENSITIZATION TO MEATS

	Number Tested	Number Positive	Questionable Number	Number Negative
Beef.....	25	0	0	25
Chicken.....	25	0	0	25
Lamb.....	25	0	0	25
Pork.....	25	0	0	25
Veal.....	25	0	2	23

TABLE 10.—CASES GIVING HISTORY OF ANAPHYLAXIS TESTED FOR SENSITIZATION TO MEATS

	Number Tested	Number Positive	Questionable Number	Number Negative
Beef.....	50	3	2	45
Lamb.....	48	2	0	46
Veal.....	33	0	0	33
Pork.....	36	0	0	36
Chicken.....	45	3	2	40

TABLE 11.—CASES GIVING NO HISTORY OF ANAPHYLAXIS TESTED FOR SENSITIZATION TO NUTS

	Number Tested	Number Positive	Questionable Number	Number Negative
Almond.....	11	0	0	0
Peanut.....	22	0	0	0
Brazilnut.....	17	0	0	0

TABLE 12.—CASES GIVING HISTORY OF ANAPHYLAXIS TESTED FOR SENSITIZATION TO NUTS

	Number Tested	Number Positive	Questionable Number	Number Negative
Peanut.....	17	0	0	17
Almond.....	11	0	0	11
Brazilnut.....	17	1	1	15

TABLE 13.—CASES GIVING NO HISTORY OF ANAPHYLAXIS TESTED FOR SENSITIZATION TO FRUITS

	Number Tested	Number Positive	Questionable Number	Number Negative
Banana.....	25	0	0	25
Grapefruit.....	25	0	0	25
Strawberry.....	25	1	1	23
Orange.....	25	0	0	25

TABLE 14.—CASES GIVING HISTORY OF ANAPHYLAXIS TESTED FOR SENSITIZATION TO FRUITS

	Number Tested	Number Positive	Questionable Number	Number Negative
Banana.....	16	0	1	15
Orange.....	10	0	0	10
Grapefruit.....	16	0	2	14
Strawberry.....	21	2	3	16

TABLE 15.—SUMMARY OF POSITIVE REACTIONS IN THE NORMAL CONTROL CASES

	Positive Reactions	Questionable Reactions	Total Positive and Questionable
Onion.....	1	0	1
Squash.....	0	1	1
Spinach.....	0	1	1
Potato.....	1	0	1
Egg white.....	1	0	1
Salmon.....	4	1	5
Codfish.....	0	2	2
Haddock.....	0	1	1
Lobster.....	0	1	1
Corn.....	1	0	1
Rye.....	1	0	1
Buckwheat.....	0	2	2
Veal.....	0	2	2
Strawberry.....	1	0	1

These articles of diet which give a positive or questionable reaction in apparently normal cases is significant in that it includes many of the common articles of diet which pediatricians usually avoid in regulating diets of children, because of experience, that they cannot be tolerated. The presence of sensitization in the absence of symptoms, may be due to a low degree of sensitization not sufficient to cause anaphylactic manifestations.

Thus it is evident from these tables that the incidence of sensitization of apparently normal children is almost a negligible factor, except in the case of salmon, which reaction in any case cannot be considered as an absolute indication of sensitization. The articles of diet most commonly causing disturbance in children presenting anaphylactic symptoms are:

- | | | |
|------------|-----------|---------------|
| 1. OATMEAL | 4. PEAS | 7. BEEF JUICE |
| 2. POTATO | 5. RICE | 8. CHICKEN |
| 3. EGGS | 6. CASEIN | |

This does not mean that a child with anaphylactic symptoms is not capable of taking any one or all of these articles of diet. Only a careful examination can reveal the causative factor. In many instances it is only one food while it may be several.

It is only by the most careful study and examination of the case, with a definite knowledge of reading the specific reactions, that the form of sensitization can be determined.

FOREIGN BODIES IN THE AIR AND FOOD PASSAGES *

EDWIN E. GRAHAM, M.D.

PHILADELPHIA

During the past two years, through the courtesy of Dr. Chevalier Jackson, I have had an opportunity of seeing in children a comparatively large number of cases of foreign bodies in the air passages, and a much smaller number of cases of foreign bodies in the food passages. I feel much indebted to Dr. Jackson for the opportunity of studying these cases, as all of them were referred to him, and he later referred them to me for medical examination as to the location of the foreign body and for medical treatment.

The subject has been of such great interest to me, and has taught me so much that I feel it may interest you if I draw attention to some of the points that seem to me most important in connection with these foreign body cases.

Of the comparatively large number of cases that I have been seeing, I have selected some of the most interesting. A brief summary of the clinical history of four of these cases will suffice to illustrate their nature.

REPORT OF CASES

CASE 1.—James W. F., aged 4 years, was admitted to Jefferson Hospital, April 19, 1919. Diagnosis: Carpet tack in right lung. Location of foreign body: lower lobe of right lung. Tack aspirated, March 15, 1919. Two previous unsuccessful bronchoscopies. Foreign body removed by Dr. Chevalier Jackson, April 23, 1919. Time: thirty-five minutes, ten seconds. Uneventful recovery. Discharged, April 26 (Fig. 1).

CASE 2.—Frank S., aged 2 years, was admitted to Jefferson Hospital, March 19, 1919. Diagnosis: Peanut kernel in right bronchus. Location of foreign body: right bronchus at orifice of upper lobe bronchus. Peanut aspirated, March 16, 1919. Symptoms: Marked wheezing, cyanosis, severe cough, fever. Tracheotomy: March 20, 1919. Kernel removed by Dr. Chevalier Jackson, March 25. Time: four minutes, twenty-six seconds. Recovery (Fig. 2).

CASE 3.—William B., aged 4 years, admitted to Jefferson Hospital, Dec. 20, 1917. Diagnosis: Staple in left bronchus. Location of foreign body: in left main bronchus. Staple aspirated, Dec. 14, 1917. Foreign body removed by Dr. Chevalier Jackson, Jan. 8, 1918. Time: eighteen minutes, fifty seconds. Recovery. Discharged, January 11 (Fig. 3).

CASE 4.—Nathaniel M., aged 8 years, admitted to Jefferson Hospital, Jan. 8, 1919. Diagnosis: Cartridge blank in left bronchus. December 24, patient aspirated empty cap of a 22 caliber bullet. Location of foreign body: at orifice of left upper lobe bronchus. Foreign body removed by Dr. Chevalier Jackson, January 11. Time: eight minutes, thirty-one seconds. Recovery (Fig. 4).

* President's address, read before the American Pediatric Society, Atlantic City, N. J., June 16, 1919.

It seems only plausible to believe that if one man can see more than seven hundred foreign body cases, and this has been the experience of Dr. Jackson, that very many foreign body cases terminate in death without a correct diagnosis being made, and without any attempt at removal of the foreign body by endoscopy.

The period of latency of symptoms which follows the primary violent dyspnea and choking attack, and later the gradual onset and chronic character of the symptoms suggest to the clinician some acute or chronic pulmonary disease, consequently one not accustomed to the study of these cases might fail to suspect the presence of a foreign body in the lung.

When one reads the histories of these children, their being referred from one competent physician to another, one is struck by the fact that in spite of the history given by the parents of having swallowed or inhaled a foreign object, little attention is paid to this fact, and very often a roentgenogram of the chest is not taken. One of the important lessons I have learned in the last two years from the study of these cases is to suspect a foreign body in the lung, if the following conditions are present: localized lung symptoms that persist in spite of treatment, no tubercle bacilli in the sputum, a leukocytosis for which there seems no definite reason, and a gradual failure in health and weight.

Foreign bodies in the lungs have been regarded practically as curiosities. So far as I can remember only one paper has been read before this society on this subject, and that some years ago. In it, if I remember correctly, three cases were reported, and in the discussion I reported two or three cases that I had found accidentally.

The symptoms of a foreign body in the air passages vary largely, depending on the nature of the foreign body. The peanut kernel immediately sets up a violent dyspnea and an accumulation of purulent secretion in the lungs due to the severe laryngitis, tracheitis, and bronchitis. On the other hand, the inhalation of a metallic foreign body, such as a tack, produces for a very short time violent dyspnea and choking after which there is a period of quiescence in which the patient is entirely free from symptoms for weeks or even months.

The period of quiescence is followed by gradually failing health and strength, cough, moderate fever and a clinical picture that suggests incipient tuberculosis. Undoubtedly foreign body cases have often been so diagnosed.

Metal objects, if they block a bronchus completely, cause a retention of the secretions and may quickly form an abscess. If, however, they occlude the bronchus only partially and the secretions can be coughed up, they may remain for a very long time and do comparatively little damage. The swelling of the mucous membrane, which is always

associated, is a factor which ultimately assists greatly in the blocking up of the secretions.

Foreign bodies in children are associated with a large amount of secretion. This excess of secretion is probably due both to the fact that the child's lung is more susceptible to the presence of a foreign body than the adult's is, and the fact that the child cannot, like the adult, remove the secretion by coughing. Statistics tend to show that about 66 per cent. of the cases of foreign bodies in the air passages occur in children, due, in my opinion, to the fact that children are very apt to put any and all objects into the mouth and exercise less care in removing them from the mouth than does the adult.

If in the history of the case there is no such history of dyspnea and choking, and one is sure that these symptoms were never present, it is a strong argument against the inhalation of a foreign body.

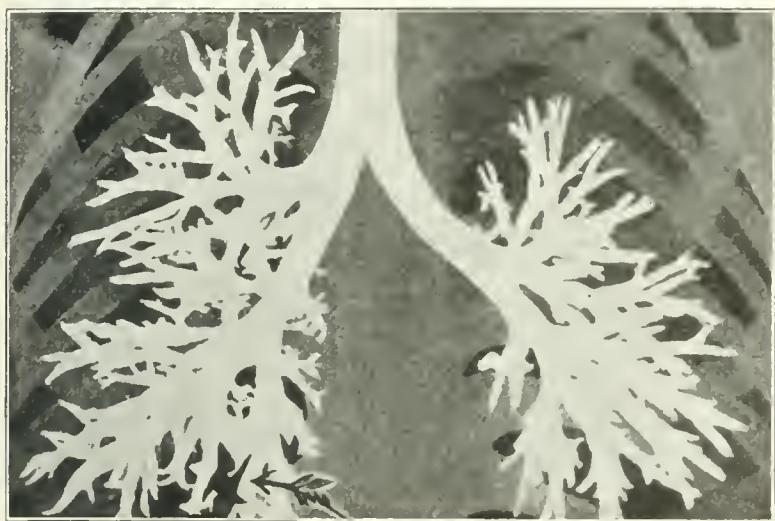


Fig. 1.—Carpet tack in lower lobe of right lung.

Food substances, such as bread, lean or fat meat, or those that are apt to be more or less quickly dissolved are usually coughed up and, as a rule, produce no dangerous symptoms. Fine particles of dust are ordinarily coughed up, but large particles, such as coal dust, often become encysted, producing anthracosis. The larger bodies may and probably do produce many of the pulmonary abscesses that are non-tuberculous.

In all foreign body cases a physical examination of the child's entire body, especially of the chest, is most important. Some foreign bodies do not cast a shadow on a photo-sensitized plate, and the study

of a large number of such cases ought to be of value. The lung symptoms are nearly always most marked in the lung containing the foreign body. The study of the physical signs, both before and after bronchoscopy, is of importance. The large amount of secretions sometimes removed by the bronchoscopy may cause the signs of consolidation in a lung to disappear. This accumulation of secretions is apt to occur in the lower lobe of the lung, and from a study of a number of such cases it is evident that the secretions gradually accumulate in this lower lobe by gravity, this accumulation taking place in spite of efforts to remove it by coughing.

If a foreign body is present in the esophagus, food may be swallowed easily and regurgitated, or swallowed with difficulty, as is the case in stricture of the esophagus. This is probably due to an associated spasm of the esophagus in the majority of cases, or less often to the change in the position of the body in the esophagus. Sometimes it is impossible to decide on the location of the foreign body in the esophagus from the sensations of the patient. Foreign bodies in the larynx usually produce hoarseness, with a croupy cough and evidences of severe dyspnea. This signifies either glottic or subglottic lodgment.

The asthmatoïd wheeze which may be heard in some of the foreign body cases, is, when present, a symptom of considerable importance, especially in those cases where the foreign body does not show a shadow on the plate. It is heard during or at the end of expiration, by placing the ear or stethoscope in front of the mouth of the patient.

It is ill advised to urge a patient to cough with the hope of expelling the object inhaled. The possibility of his coughing it up is very slight, and the probability of his doing injury by forcing the sharp point of the object inhaled, such as a tack, into the laryngeal mucosa is very great.

A larger number of foreign bodies enter the right than the left bronchus, from 62 to 75 per cent. according to different observers. Consequently more foreign bodies lodge in the right lung than in the left, and they rarely lodge in the middle lobe bronchus. There are good anatomical reasons for this, as the diagram from Dr. Jackson's book clearly shows (Fig. 5):

The right bronchus is larger than the left, and the angle of deviation is less acute; and the carina, i. e., the top of the bifurcation, is to the left of the middle line of the trachea.

Heavy objects, owing to their weight in comparison to their small size, are rarely coughed up. In fact, very light substances, such as cork, are rarely spontaneously removed by coughing, and the consensus of opinion today is to remove the foreign body by endoscopy.

The physical signs of foreign bodies that have localized themselves in the lung depend on the amount and extent of the lesions. They may vary according to the composition, form, shape and size of the foreign body, as to whether it blocks the bronchus slightly, largely or completely, and also, to a certain extent, on the amount and character of the secretions. There may be a simple local bronchitis, slight or severe local congestion, slight or much retained purulent secretions, bronchiectasis, or pulmonary abscess. When the foreign body has been present for a long period of time, there is usually a moderate degree of bronchitis in the opposite lung, probably due to the retained secretions gaining access to the other lung, but with the exception of the peanut and maize cases, the local evidences around the foreign body are so well marked that they are usually easily recognized, espe-

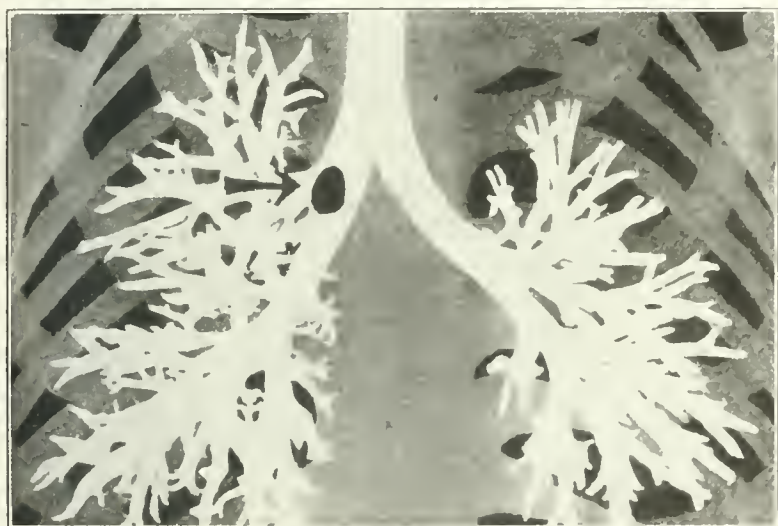


Fig. 2.—Peanut kernel in right bronchus.

cially in those cases where the foreign body has been present long enough to produce distinct local pathology. In a case where a foreign body has been present in the lung for a long period of time there is usually considerable cough with offensive expectoration.

If a cavity forms, it may be either a bronchiectatic or an abscess cavity, and there is an absence of tubercle bacilli in the sputum. In a recent case the expectoration is less offensive and more of a mucopurulent character, and occasionally streaked with blood.

Dr. Jackson speaks often of "drowned" lung in his foreign body cases. In a number of cases it is noticed that a great deal of opacity in the tissues surrounding the foreign body disappears after bronchos-

copy. This is evidently due to the copious outpouring of secretions after the bronchoscopy. In some of the cases where the foreign body has been present for a number of years, some evidences of damage to the lung may still be visible in the roentgenogram months after the object has been removed, although at this period all physical signs have disappeared clinically. A "drowned" lung, according to Dr. Jackson, is caused by the drainage becoming blocked by the foreign body. The passages of the lungs become filled with secretions, which collect easily, and these consequently become purulent. If this area of drowned lung is not relieved by the removal of the foreign body from the bronchus, we have finally an abscess cavity.

Foreign bodies are occasionally coughed up. It is more likely to be coughed up if the object is in the larynx than if it is in the bronchi. The possibilities of a foreign body being coughed up are very slight, however. The nature of the foreign body has something to do with it. Pins and sharp bodies are rarely if ever expelled by coughing, as the effort of coughing causes the sharp point to become more tightly fixed. Round, smooth objects usually become firmly lodged, the air below the object is absorbed and coughing consequently can hardly ever be strong enough to disturb the foreign body, as little air is below it. Heavy bodies, as stated before, are seldom coughed up.

According to the experience of Dr. Jackson, pins are the most common foreign bodies in the bronchi, next in frequency are different kinds of hardware, then vegetable substances.

If there is any reason to suspect a foreign body, a bronchoscopy should be performed. It is important to appreciate that a foreign body does not necessarily produce any physical signs or symptoms, and, on the other hand, it is important to remember that certain lesions in the air passages, as a false membrane, may closely simulate the physical signs and symptoms of a foreign body.

In a case of suspected bronchiectasis, a bronchoscopy may assist in clearing up the diagnosis, especially if the symptoms are limited to one base and are suggestive of tuberculosis, but no tubercle bacilli are found.

There are no contraindications to bronchoscopy, except, perhaps, extreme weakness of the patient, when time should be given the individual to rally partially. Pulmonary abscess, pneumonia, pulmonary gangrene or status lymphaticus, are not contraindications for bronchoscopy.

Bronchoscopy should be performed as soon as possible after the entrance of the foreign body. The longer the time that elapses, the more difficult is the removal owing to the swelling and edema of the bronchial mucosa, later the formation of granulation, and also the

fact that the natural tendency of the foreign body is to sink deeper and deeper into the lung.* The child's health and strength gradually become impaired, which, of course, tends to make convalescence more tedious.

I have never seen Dr. Jackson give an anesthetic to children, although we have occasionally given a small dose of morphin with atropin to older children before the bronchoscopy.

The necessity of making a roentgenogram in every case in which a history of having swallowed or inhaled a foreign body is given cannot be emphasized too strongly. If a suspicion exists that a foreign body may be present, a roentgenogram should be made, or if an unexplained leukocytosis is present, connected with local physical

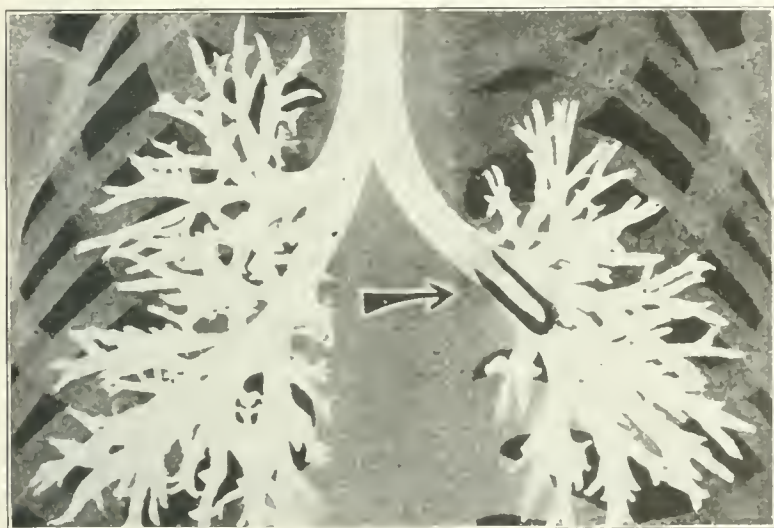


Fig. 3.—Staple in left bronchus.

signs in the lungs that do not clear up under treatment, and if there are no tubercle bacilli in the sputum, the necessity for taking a roentgenogram is evident. It is difficult to explain why so many patients with definite local lesions in one lung that are nontuberculous and that do not disappear under treatment, are not given the benefit of roentgen-ray examination. The probable explanation is that the medical profession, as a whole, does not appreciate the frequency of foreign bodies in the lungs, and the history of having swallowed or inhaled a foreign body is disregarded owing to the period of latency which exists between the time of inhalation and the first development of symptoms.

In a roentgenogram one side may be dark and the other side light. The dark side usually contains the foreign body, perhaps occluding a

large bronchus, which may produce a well marked emphysema in the unobstructed lung. It is well to remember that calcified glands may show a rounded shadow.

It is important to appreciate that a negative roentgenogram does not absolutely prove that a foreign body is not present. Metal objects may not show, or the object may not be opaque to the roentgen ray. The physical signs in such a case are often a valuable guide.

The location of a foreign body in the esophagus that shows but slightly, if at all, in the roentgenogram may be facilitated by having the patient swallow a capsule containing bismuth. This capsule may lodge just above the foreign body. It is important to remember that in a perfectly free esophagus the capsule may stop for a moment in its passage through the esophagus.

If the foreign body is in the lung, the bronchoscope, and if in the esophagus, the esophagoscope is used. Both are passed through the mouth. The illumination is at the distal end, and all the work is done by sight: nothing is done in a blind manner.

The extraction of foreign bodies of steel or iron by the magnet has very narrow limitations, practically only such bodies can be removed as are easily removed by bronchoscopic means.

The bronchi do not diminish in size between the branches. The lessening in the lumen occurs at the point of subdivision between the branches. The lumen between the branches is of a uniform size and does not taper, consequently a foreign body usually is checked and stops below where branching begins.

The diagnosis is made from the history of a foreign body being in the mouth, with an attack of violent dyspnea, and choking sensations. Except when substances such as a peanut kernel or maize is inhaled, this is followed by a period of quiescence and freedom from all symptoms that often lasts for weeks or months. The physical signs are largely localized to a comparatively small area in one lung.

As regards prognosis, Dr. Jackson reports 98.1 per cent. successful removals. His mortality during operation is less than 0.5 per cent. Including all deaths within one month after endoscopy in more than 700 cases, his mortality is 1.9 per cent. Even this low mortality, if studied carefully, will be found to be due almost entirely to the fact that the patients either were almost moribund when the attempt to remove the foreign body was made, or else the object had been present in the lung so long that notwithstanding its removal the patient later succumbed to the lung condition.

In Jackson's twenty-three cases where the foreign body had been present for from two months to twenty-six years, there were two deaths. The recovery from the pulmonary conditions present is, as a

rule, complete, as far as symptoms are concerned. Cough, expectoration and fever disappear, the child gains in weight and strength, and recovery is apparently complete. The later roentgenologic study of the lungs in these cases also shows a remarkable and to the clinician often an unexpected recovery.

In regard to prophylaxis, all children should be prevented as far as possible from putting any object in the mouth, and when old enough they should be taught the danger of putting objects in the mouth. Great care should be taken that no foreign body gains access to the food before it is eaten. Bones, pins and numerous small objects, such as china and glass, are found in foodstuffs, and as a result may be swallowed or inhaled, if not noticed during mastication. It is most

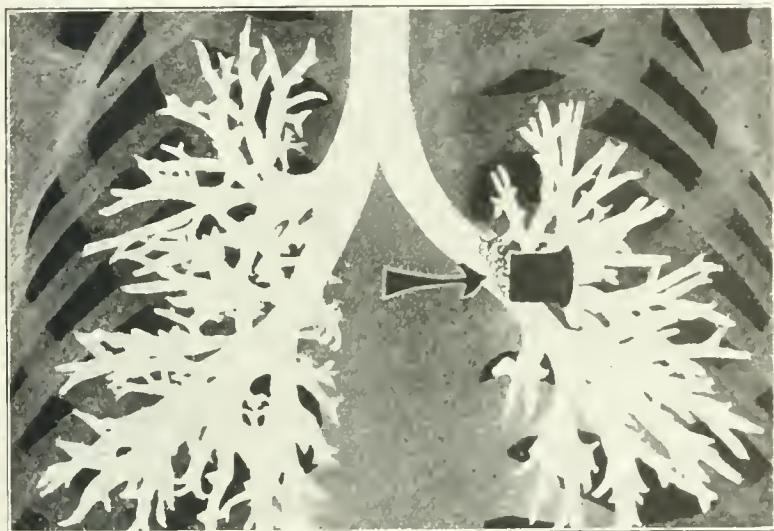


Fig. 4.—Cartridge blank in left bronchus.

important not to leave objects small enough to be placed in the mouth lie where young children can pick them up. A good sized safety pin is not too large to be placed in the mouth of the young child, and possibly swallowed or inhaled.

In children less than 2 years of age a bronchoscopy should not last more than thirty minutes, unless it is urgently required to prolong it, when it may last for one hour. Children more than 2 years of age will easily stand a bronchoscopy lasting one hour. This is done without either general or local anesthesia, although occasionally a small preliminary dose of morphin and atropin is given. Many of Dr. Jackson's operations for removal of foreign bodies are done in two or three minutes.

As regards treatment, with an early roentgen-ray examination and a bronchoscopy, the treatment is most satisfactory. If a foreign body is inhaled, the patient should be kept as quiet as possible, and as much in the recumbent position as possible, until after the larynx has been examined by the mirror and a roentgenogram has been taken. The idea in keeping the patient recumbent is to keep the foreign body from gravitating lower into the lung. It is important to quiet the patient as much as possible, and he should never be urged to cough with the idea of possibly coughing up the foreign body. It is never wise to pass a bougie into the esophagus for the location of a foreign body or where disease is present. The passage of the bougie practically gives us very little knowledge, and the passage of the esophagoscope, which is certainly no more difficult, gives us valuable knowledge. As a second "don't" to the passage of the bougie might be mentioned the fact that the child should never be held up by the heels and slapped on the back, as there is danger of the foreign body becoming detached, and asphyxiation may result from the object becoming caught in the glottis. Of course, it goes without saying that in all cases of foreign body a roentgenogram should be taken, and taken as early as possible.

All children should be kept in bed and, if possible, under a competent nurse for several days after the foreign body is removed.

As a rule, there is little or no fever after the bronchoscopy, although at times the temperature rises to 100 F. Usually, even in these cases, it falls to normal in a day or two. This was a matter of surprise to me in the first few bronchoscopies that I saw Dr. Chevalier Jackson do, as I expected fever and cough to follow the passage of the bronchoscope, and the manipulation with the instruments necessary to remove the foreign body. The instruments used are, of course, all sterile, and the sensitiveness of the deeper bronchi is very slight as compared with the larynx, hence the child stands the necessary intrusion of the deeper structures well and there can be no infection, as no local or constitutional symptoms follow the operation. If pneumonia is present before the bronchoscopy there may be a severe reaction, although in none of such cases that I have seen has it been fatal.

If before the bronchoscopy, a bronchitis, tracheitis or laryngitis with fever is present, these symptoms are usually aggravated temporarily by the bronchoscopy. The reaction was most marked in the peanut cases. If the epithelium is injured either by the foreign body or by the necessary manipulation, the reaction may be severe following the passage of the bronchoscope. A moderate degree of hoarseness is often seen in children, which usually lasts only two or three days. What Dr. Jackson speaks of as a "drowning of the patient by his own secretions" has been noted in a number of cases in children, especially

in the peanut cases. This is usually relieved by the passage of the bronchoscope, and the "sponge pumping" process.

Subglottic edema may be present before the bronchoscopy, due in some cases to the presence of a foreign body in the subglottic region, or in the trachea, or it may be caused by the cough or respirations moving the foreign body backward and forward. Jackson believes that distal illumination and the use of small tubes lessens the risk of the production of this edema of the glottis. If the symptoms are due to subglottic edema a low tracheotomy gives great relief, as I have seen in a number of cases. The tube can usually be removed in a comparatively few days.

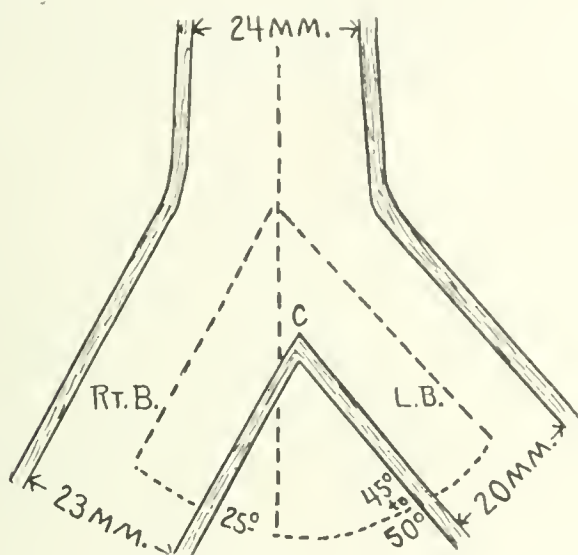


Fig. 5.—Diagram showing three anatomic reasons for the greater frequency of right sided lodgment of foreign bodies in the bronchi. The right bronchus (Rt. B.) is almost as wide (23 mm.) as the trachea (24 mm.), and it deviates from the long axis of the trachea much less than the left. The carina (C) is to the left of this axis. (After Sir St. Clair Thomson.)

CONCLUSIONS

1. It seems reasonable to believe that foreign bodies in the air and food passages in children are much more common than was formerly supposed. Statistics tend to show that about 66 per cent. of these cases of foreign bodies in the air passages occur in children.

2. The period of latency of symptoms which follows the violent dyspnea and choking attack, and later the gradual onset, and chronic character of the symptoms, might lead one to fail to suspect the presence of a foreign body.

3. Foreign bodies are certainly often overlooked, as a study of the histories of many cases clearly shows.

4. The symptoms vary greatly. The peanut kernel immediately sets up a severe laryngitis, tracheitis and bronchitis. In the peanut cases, the older child may survive the acute symptoms, but almost surely will develop pneumonia.

5. Metal objects may remain in the lung for a very long while and do comparatively very little damage.

6. There are some foreign bodies that do not cast a shadow on the plate.

7. The location of a foreign body in the esophagus that does not cast a shadow on the plate may often be diagnosed by allowing the patient to swallow a bismuth filled capsule. The roentgen ray shows the location of the bismuth capsule held in position in the esophagus by the foreign body.

8. Do not urge the patient to cough with the hope of expelling the foreign body inhaled in the lungs.

9. Foreign bodies are very rarely coughed up.

10. The physical signs and symptoms vary according to the composition, form, shape and size of the foreign body.

11. One should suspect a foreign body if the following conditions are present: an unexplained leukocytosis, localized symptoms in one lung that do not clear up under treatment, no tubercle bacilli in the sputum, and a gradual failure in weight and strength.

12. There are no contraindications to bronchoscopy except, perhaps, extreme weakness in the patient, when time should be given the individual to rally partially.

13. Bronchoscopy should be performed as soon as possible after the entrance of the foreign body.

14. Children do not require the administration of an anesthetic for the performing of a bronchoscopy.

15. The necessity of taking a roentgenogram in every case with a history of swallowing or inhaling a foreign body, cannot be emphasized too strongly.

16. The asthmatoïd wheeze, when present, is a sign of considerable importance.

AURICULOVENTRICULAR HEART BLOCK IN CHILDREN

WITH REPORT OF A CASE *

J. A. E. EYSTER AND W. S. MIDDLETON

MADISON, WIS.

Cases of auriculoventricular dissociation in children that have been studied and described are summarized in the accompanying table. The case to be described in the present paper is also included. It would seem from the relatively small number of cases that a search of the literature has revealed that this condition is either much less common or is more frequently overlooked in children than in adults.

The diagnosis in Cases 1, 2, 3, 4, 11 and 16 was made by the ordinary methods of physical examination or inferred from the history of slow pulse and syncopal attacks. It must be accepted, therefore, with a certain amount of reservation. In the other cases, the condition was definitely constituted by either jugular pulse tracings or electrocardiographic records.

Probably the first case reported was that by Schuster, which the author states was one of bradycardia of unknown nature following acute rheumatic fever. Attacks occurred which simulated the Stokes-Adams syndrome, but were not absolutely typical. The pulse rate was normal between attacks. There was associated mitral insufficiency and extensive cardiac enlargement.

It will be noted that a large proportion of the cases reported occurred during severe and usually fatal cases of diphtheria. This group includes six of the twenty cases that we have been able to find in the literature. Five of these cases had a fatal termination. The predilection of the diphtheria toxins for heart muscle is well recognized clinically, and disturbances of the conduction system of the heart would probably be found more frequently if more carefully watched for in this disease. In addition to the cases summarized, two probable cases of heart block in eleven fatal cases of diphtheria studied by Rohmer¹ might be included. Because of some doubt as to the diagnosis and the absence of sufficient clinical data in regard to these cases, we have not included them in the summary. Further, in a series of fifteen fatal cases of diphtheria in which the hearts were subjected to careful pathologic study by Tanaka,² the case report on one indicated complete dissociation with the Stokes-Adams syndrome.

* From the medical clinic of the University of Wisconsin

1. Rohmer: *Jahr. f. Kinderh.* **76**:39, 1912.

2. Tanaka: *Virchows Arch. f. path. Anat.* **207**:115, 1912

The largest group of cases, nine in number, comprise those in which the cause of the disturbed conduction is ascribed to a congenital defect in the conductive system. The familial tendency in congenital cases has been emphasized by Marquio and by Fuller, Judson and Norris. Marquio's cases occurred in a family of eight children, five of whom manifested symptoms of Stokes-Adams' disease, beginning in all cases at 4 years of age and leading to the death of four of these patients before the ninth year. The fifth patient was still alive at 5 years of age. One of the three who showed no evidences of the disease died of typhoid fever at 6 years of age, one was 2 years old and thus below the age of manifestation of the disease in this family and one was 17 years of age and had shown no evidences of the disease. The father and mother were in good health with apparently normal hearts. The father and one sister of the case described by Fuller, Judson and Norris showed partial auriculoventricular dissociation and another daughter, although the heart was apparently normal at the time of examination, gave a history of previous attacks closely resembling the Stokes-Adams' syndrome.

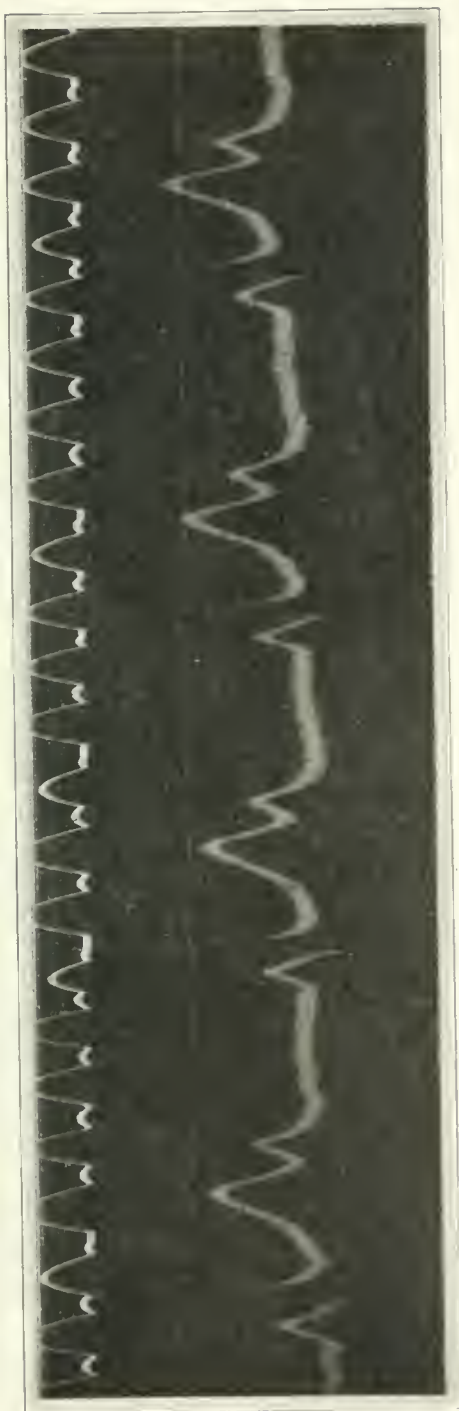
Of the remaining cases, one (Case 1) was associated with a severe mitral lesion resulting from acute articular rheumatism; one case (Case 12) was ascribed to the presence of a primary cardiac tumor believed to have its origin in the auriculoventricular node, and in one case (Case 17) the condition was discovered during a severe attack of whooping cough and bronchitis. In one case (Case 13) there was a history of measles four years and "inflammation of the heart valves" one year previous to the examination. Finally, Case 19 apparently developed during an acute febrile attack of undetermined nature.

The case forming the subject of the present report is one of partial auriculoventricular dissociation which has been under observation for more than two and a half years.

REPORT OF CASE

CASE.—A male child, aged 2 years, was referred by Dr. H. E. Purcell of Madison, Jan. 26, 1917, because of cardiac murmur and irregularity of rhythm. The family history is unimportant. The child was delivered by low forceps after normal pregnancy and at full term, and appeared normal up to the onset of the present trouble, although no cardiac examination was made previous to this time. The present illness began January 16 with an acute nasal and tonsillar infection, and examination by Dr. Purcell on the third day of the illness revealed the cardiac arrhythmia and murmur.

On examination the pulse was somewhat irregular, averaging about 75 per minute, and a soft systolic murmur was heard at the apex, transmitted to the midaxillary line, but not heard at the base. Electrocardiograms showed increase in auriculoventricular conduction and blocked auricular beats every third or fourth cycle. The temperature was normal. The tonsils were enlarged, particularly the left, which was also deeply congested. Other examinations were negative. There were no indications of congenital heart disease. Examinations on successive days showed an increase in the degree of heart block



2:1 Atriculoventricular heart block.

and an increase in the loudness and transmission of the murmur. Electrocardiograms made January 30 revealed a 2:1 auriculoventricular block, with a ventricular rate of 62. Roentgenograms showed enlargement of both ventricles and of the left auricle, with a total area of 57 sq. cm., corresponding, according to Bardeen's tables, to the normal for 8 years of age and a body weight of 48 pounds. There was considerable cyanosis of the head and of the body.

In view of the increase in the degree of block, change in character and transmission of the murmur and cardiac enlargement, it was believed that the pathologic process was definitely progressing. Because of the probable association of the tonsillar infection with the condition, tonsillectomy was performed February 2 under ether anesthesia. Cultures from the tonsils revealed *Staphylococcus aureus*. Following the operation, the condition improved steadily. February 7, the cyanosis had disappeared completely. The heart block was less, only every third or fourth auricular impulse failing to reach the ventricle. The pulse rate was 77. February 14, electrocardiograms showed a 3:2 heart block with a ventricular rate of 82. The extent of the block still further decreased and June 2, only every third or fourth beat was blocked. The murmur became soft and distant, and its area of propagation was reduced, being confined to the apex and its immediate vicinity. The cardiac size was reduced to 50½ sq. cm.

The child has been in good health since this time, has developed normally and manifests normal activity. July 20, 1919, a soft systolic murmur could be heard at and in the immediate neighborhood of the apex. The heart was moderately enlarged; the rate of beat was about 57 per minute and force and rhythm were regular. Electrocardiograms showed a 2:1 auriculoventricular heart block, as is shown in the accompanying illustration.

Administration of atropin in full doses increases slightly the rate of both auricles and ventricles but does not affect the degree of block. The depression of conductivity in the bundle is, therefore, not due to hypervagotonus.

DISCUSSION

The electrocardiograms at the first examination showed the mildest type of auriculoventricular heart block. Auriculoventricular conduction following a blocked beat was normal (from 0.14 to 0.16 second). There was then an increase in conduction time in the next two or three cycles, 0.30 to 0.32 second, and following this, conduction fails for one cycle. This condition passed a few days later into a condition of 2:1 block in which, however, occasionally two auricular beats in succession were conducted through to the ventricles. When the latter occurred, the period of auriculoventricular conduction in the second cycle was greatly prolonged. This increase in the extent of the block was associated with increase in the extent and distribution of the murmur, and evidences of deficient circulation (cyanosis) due to the slow ventricular rate. Following tonsillectomy, the conductivity of the auriculoventricular bundle improved, and with it the general condition of the patient. There was not, however, complete restoration of normal conductivity. Subsequent to this, the block again increased, without, however, any apparent interference with health and development. July 20, 1919, it was a 2:1 block with the occasional propagation of two successive auricular beats. When the latter occurs, the period of conduction in the second cycle is greatly prolonged. The character and

SUMMARY OF CASES RECORDED IN THE LITERATURE

Case	Date	Author	Reference	Age	Sex	Disease	Nature of Block	Character	Duration	Ventricular Rate	Termination	Stokes-Adams Syndrome
1	1896	Schuster.....	Deutsch. med. Wchnschr., 22:484	4 yrs.	M	Rheumatism	?	Recurrent	3 mos.	35	Present?
2	1901	Marqule.....	Arch. de med. d. enf., 4:467	8 yrs.	M	Congenital	Complete?	Continuous	4 yrs.	50-70	Death	Present
3	1901	Marqule.....	Arch. de med. d. enf., 4:467	5 yrs.	M	Congenital	Complete?	Continuous	18 mos.	50-70	Present
4	1903	v. Stark.....	Monatschr. f. Kinderh., 2:11	5 yrs.	M	Congenital	Complete?	Continuous?	1 yr.	28-44	Death	Present
5	1908	Dunn.....	J. A. M. A., 50:1985	11 yrs.	M	Diphtheria	?	Continuous?	3 days	18-40	Death	Present
6	1908	v. d. Heuvel.....	Proefschr. v. Groningen	13 yrs.	F	Congenital	Complete	Recurrent	11 yrs.	34	Present
7	1910	Fulton, Judson and Norris	Am. J. M. Sc., 140:339	2 yrs.	M	Congenital	Complete	Continuous	40-50	Absent
8	1910	Magnus-Alsleben.....	Ztschr. f. klin. Med., 69:82	8 yrs.	M	Diphtheria	Complete	Recurrent	5 days	29-38	Death	Present?
9	1910	Fleming and Kennedy	Heart, 2:77	10 yrs.	F	Diphtheria	Complete	Continuous	3 days	40-54	Death	Absent
10	1911	Price and Mackenzie	Heart, 3:253	9 yrs.	F	Diphtheria	Complete	Continuous	5 days	34-48	Death	Absent
11	1911	Hellmecker.....	Ztschr. f. Path., 8:319	14 yrs.	M	Diphtheria	Complete	Recurrent	3 days	5	Recovery	Present
12	1911	Armstrong and Monckeberg	Deutsch. Arch. f. klin. Med., 102:143	5 yrs.	M	Cardiac tumor	Complete	Recurrent	18 mos.	28	Death	Present
13	1914	Hocht.....	Wien. med. Wchnschr., 64:178	9 yrs.	M	?	Complete	Continuous	3 yrs.?	40	Present
14	1914	Hocht.....	3 yrs.	M	Diphtheria	Partial, later complete	Continuous	6 mos.	30-60	Recovery	Present
15	1915	d'Espine.....	Bull. de l'Acad. de med., 14:372	8 yrs.	M	Congenital	Complete	Continuous	1 mo.	20-32	Present
16	1915	Zuborsky.....	Interstate M. J., 22:57	15 mos.	F	Congenital	Complete	Continuous	14 mos.	50	Present
17	1915	Whipple.....	Brit. J. Child. Dis., 12:321	18 mos.	F	Bronchitis	Partial	Continuous	8 mos.	56-64	Absent
18	1915	Whipple.....	Brit. J. Child. Dis., 12:321	12 yrs.	F	Congenital?	Complete	Continuous	6 yrs.?	40-64	Absent
19	1916	Frank and Polak.....	Niederlandsch. Tijdschr. v. Geneesk., 52:2172	2 yrs.	F	Pyogenic	Complete	Continuous	42-48	Absent
20	1918	Bass.....	J. A. M. A., 70:287 (Feb. 2)	15 yrs.	M	Congenital	Complete	Continuous	37	Absent
21	1919	Lyster and Middleton	2 yrs.	M	Pyogenic?	Partial	Continuous	2½ yrs.	58	Absent

distribution of the systolic murmur, and the size and shape of the heart, indicate the presence of a well compensated mitral lesion.

It seems to us that one of two possible explanations can be given to the present case. The first is that of a congenital heart lesion of unknown nature, complicated by a lesion or imperfect development of the His bundle. Opposed to this is the probable absence of a murmur until the onset of the acute infection at 2 years of age, although careful physical examination had not been made previously, the atypical character of the shape of the cardiac outline, and the absence of any of the usual signs or symptoms of congenital heart disease. The second possible explanation is a myocardial focus of infection, possibly associated in its development with the attack of tonsillitis. The rapid increase in the extent of the block at one time, and the improvement in auriculoventricular conduction and in general symptoms subsequent to tonsillectomy, would seem to be in favor of this view of the nature of the condition. The accompanying decrease in the degree of cardiac enlargement, and the apparent absence of left auricular dilatation at present, point to the same conclusion.

SUMMARY

A case is described of partial auriculoventricular dissociation developing in a child, aged 2 years, apparently associated with an acute nasal and throat infection. This child has been under observation for more than two years. At present the cardiac condition is that of a well compensated mitral lesion, associated with a 2:1 auriculoventricular block, with a ventricular rate between 50 and 60. The child has developed normally, and is at present in apparent good health and is normally active.

A search of the literature has revealed twenty reported cases of heart block in children. Nearly all of these were definitely or probably of congenital origin or occurred during the course of severe and usually fatal diphtheria. The present case is regarded of particular interest in reference to its probable origin and the relatively mild clinical disturbance produced by the condition.

ABSCCESS OF THE LUNGS IN INFANTS AND CHILDREN

HARRY WESSLER, M.D., AND HERMAN SCHWARZ, M.D.

NEW YORK

During the past few years there have come under our observation fifteen cases of abscess of the lungs in young individuals. They are included in a series of 100 cases occurring at all ages which were previously recorded by one of us (H. W.). However, because of their special interest to pediatricians they are, perhaps, worthy of separate consideration.

ETIOLOGY

Three of these cases followed aspiration of a foreign body; five cases were subsequent to operation for tonsillectomy and seven cases may be attributed to pneumonia or other inflammatory lung conditions.

PATHOLOGY

The cases following tonsillectomy easily lend themselves to a study of the manner in which these abscesses may be produced. It is probable that during general anesthesia the purulent plugs which are expressed from the tonsillar crypts by the grasping forceps are aspirated into one of the smaller bronchi. The obstructed bronchus is further sealed by aspirated blood, which, after it has clotted, creates favorable conditions for the development of whatever anaerobic organisms may be present in the tonsillar plug.

There results a local inflammatory process, a pneumonitis, within which will always be found one or many bronchi with necrotic and dilated walls. Subsequently, the usual signs of gangrene of the lung—cough with fetid expectoration—are added.

It is difficult to determine the rôle played by the various organisms which are found in these cases. Although it is possible that streptococci and other aerobic organisms may be partly or entirely responsible for the initial pneumonitis, there is good reason to believe that from its inception, abscess or gangrene of the lung may be regarded as an anaerobic lung infection. One of the grounds for this belief is the uniform incubation period not only in the posttonsillectomy cases, but also in all other cases in which aspiration of septic material into the bronchi occurs. Thus, in thirty-five cases of aspiration abscess or gangrene, the onset of fetid expectoration invariably occurred on the thirteenth or the fourteenth day after operation or aspiration.

Evidently, general anesthesia, which was resorted to in all of our cases, stands in close relation to the production of these abscesses.

It would seem that considerations of safety would prompt the invariable use of a suction pump whenever the operation is performed under general anesthesia, as almost without exception it has proved an effectual safeguard against aspiration.

The so-called postpneumonic cases may be separated into two groups. In the first group, the patient apparently contracts a pneumonia, which runs an acute course. On the thirteenth or fourteenth day, however, just as in the cases following aspiration, the classical symptoms and signs develop. The definite incubation period and the frequency of involvement of the upper lobes, make it plausible that in these cases the mechanism is the same as in the aspiration cases. In the second group of postpneumonic abscesses, a bronchopneumonia, instead of resolving, persists, and after varying periods of time, gives rise to a chronic indurative pneumonia with multiple bronchiectases which may or may not become gangrenous. Mention should finally be made of cases of pleuropneumonic bronchiectases or abscess which may result from empyemas.

The location of the inflammatory process in the lungs varies with the etiology. In the postoperative abscesses and in the aspiration type of postpneumonic abscess, the disease is usually situated in the upper lobes. On the other hand, abscesses resulting from the aspiration of foreign bodies and the chronic bronchopneumonic type of bronchiectasis usually localize in the lower lobes. It is not improbable that the recumbent position during operation has some bearing on the upper lobe localization of these abscesses.

CLINICAL COURSE

The symptoms of acute lung abscess, taking the posttonsillectomy cases as a type, are as follows: Immediately, or several days after the operation, a distressing persistent cough develops. This is especially harassing at night, but it may also be present throughout the day. With the cough there is usually a rise of temperature. The temperature is fairly constant during the first weeks, with minor fluctuations. Later it may become intermittent, and there may be entire absence of temperature elevation for days. The physical signs of lung involvement are usually slight or absent during the early stages. Later, they may become definite, and the evidences of a cavity may be made out. This is in contradistinction to the adult cases in which the physical signs, even of an extensive process and a large cavity, are usually indefinite.

On the thirteenth or fourteenth day, signs of gangrene are noted, including fetid breath, putrid sputum and hemoptysis. The sputum is then profuse. Club fingers appear very early and disappear after the abscess has healed, sometimes earlier. During the course of the dis-

ease, complications, such as perforation of the abscess into the pleura with a resulting empyema or pyopneumothorax, severe hemoptysis or cerebral abscess, may make their appearance.

The further course of cases of abscess of the lung depends on the etiology. A survey of the outcome of more than thirty postoperative abscesses in children and adults shows that in about one third of the cases recovery occurs spontaneously. This always takes place within about two months after the onset. An abscess which lasts longer than this is apparently not susceptible of spontaneous cure. These cases go on with periods of improvement and of apparent cure. However, sooner or later other abscess cavities form, extensive induration of the lungs develops, other lobes become secondarily infected and finally, any of the complications mentioned may supervene.

ANALYSIS OF FIFTEEN CASES OF ABSCESS OF THE LUNG

Etiology	Duration	Procedure	Result
Posttonsillectomy.....	6½ mos.	Operation	Death; hemorrhage
Posttonsillectomy.....	10 mos.	Operation	Cure
Posttonsillectomy.....	7 wks.	Palliative	Cure
Posttonsillectomy.....	Operation	Death; shock
Posttonsillectomy.....	1 yr. 6 mos.	Palliative	Death; hemorrhage
Posttonsillectomy.....	5 wks.	Palliative	Death; gangrene of lung
Foreign body.....	8 yrs.	Palliative	Death; brain abscess
Foreign body.....	1 yr.	Operation	Cure
Foreign body.....	5 mos.	Bronchoscopy	Cure
Postpneumonia.....	8 mos.	Operation	Cure
Postpneumonia.....	10 mos.	Operation	Cure
Postpneumonia.....	6 yrs.	Palliative	Invalidism
Postpneumonia.....	6 yrs.	Palliative	Invalidism
Postpneumonia.....	8 yrs. plus	Palliative	Invalidism
Postpneumonia.....	6 wks.	Palliative	Cure; hemiplegia

PROGNOSIS

The prognosis is bad in the postpneumonic cases. In few of the cases is recovery spontaneous. Some of them pursue a course similar to that of the posttonsillectomy cases. In the others, usually those following influenza or bronchopneumonia, minor symptoms may be manifested for a long time. The lung induration may lead to multiple, thin walled, cylindric bronchiectases which secrete enormous amounts of purulent sputum. In such cases, in which the disease does not involve the lung parenchyma, the patient may be well for years and suffer no more discomfort than is entailed by the periodic emptying of the numerous bronchiectases. On the other hand, the supervention of anaerobic infection may at any time convert these relatively benign cases into the more severe forms. They may continue over a period of many years.

The roentgen-ray examination has been of great value, not only for diagnosis, but also for a careful and exact oversight of the progress of these cases. Thus, in view of the frequent remission in the symp-

toms of acute abscess, great caution must be observed in making any statement in regard to cure. In cases of apparent cure the roentgen-ray examination has frequently demonstrated the persistence of a small pneumonic area, which has later been the nidus of a reinfection of the lung. Of course, the exact localization of the process is of the greatest value to the surgeon who contemplates any operative procedure.

TREATMENT

Certain indications for the treatment of these cases follow logically from what has been said. In at least one third of the postoperative cases recovery occurs spontaneously up to two months, and therefore it is evident that during this period, all treatment should be palliative and will differ little from that employed in any case of pneumonia. In cases which have persisted beyond this time the question of operative procedure will arise. The extremely distressing cough and nauseating odor of the expectoration make the patients not only a burden to themselves, but to those around them, and any operation that holds out even a small hope of success is eagerly welcomed. In young persons, with their great resistance to operative shock, the very serious operation of lobectomy, in selected cases, has yielded brilliant results, and it is hoped, that with further improvement in the technic of thoracic surgery, this operation may be still further freed from its dangers. Incision and drainage of the abscess offers less hope for permanent cure, although the operation in cases may result in considerable amelioration of the symptoms.

Finally, it may be emphasized that bronchoscopy should be performed in every case of lung abscess for the detection of a foreign body. In children especially a history of the aspiration of a foreign body may not be obtained, and the roentgen-ray examination may not disclose it. Thus, on more than one occasion a localized empyema has been traced to a ruptured lung abscess at the basis of which a foreign body was found by the bronchoscopist. Early removal of such a foreign body may lead to the prompt resolution of a lung abscess if it is not of too long standing.

THE ELIMINATION OF ACETONE BODIES DURING INFECTIOUS FEVERS *

BORDEN S. VEEDER, M.D.

ST. LOUIS

AND

MEREDITH R. JOHNSTON, M.D.

Captain, M. C., U. S. Army

It has been established by numerous qualitative studies that acetone bodies are found in the urine of patients with infectious diseases. But few quantitative studies have been made in regard to this point, and these by early and rather imperfect analytical methods. As a part of a general study of acetonuria, we have collected some data in regard to the degree of acetonuria occurring in some of the infectious diseases of childhood, using the method of Schaffer for determining the quantity of acetone bodies.

Observations were made on forty-one children with scarlet fever, diphtheria, measles and pneumonia. In the majority of the observations, the collection of urine was started immediately on the admission of the patient to the hospital or after the onset of the disease. In a number, however, the infectious disease developed or was contracted during the presence of the patient in the hospital for some other condition, and complete curves from the very onset were obtained in these cases. The acetone, diacetic acid and betahydroxy-butyric acid were determined in terms of acetone.

In a previous paper¹ we showed that the healthy child eliminates on an average from 50 to 80 mg. of acetone bodies daily and the limits were from 20 to 100 mg. Accepting these figures, we find that only twenty-four of the forty-one children observed showed an increased elimination for some twenty-four hour period during the height of the disease, and in a number of them the excess was very slight. For example: D. H., scarlet fever. First day, 0.031 mg.; second day, 0.126 mg.; third day, 0.029 mg. The highest value obtained was 1.32 gm. eliminated in twenty-four hours by a patient with scarlet fever.

DEGREE OF FEVER AND SEVERITY OF INFECTION

The question next arises as to whether or not the acetonuria bears a relation to the severity of the infection. The degree of febrile reaction and the degree of prostration are the signs by which we are

* From the Department of Pediatrics, Washington University School of Medicine.

1. Veeder and Johnston: *Am. J. Dis. Child.* **13**:291 (April) 1916.

accustomed to judge the severity of infection—at least in the acute stage. Increased elimination, with a slight elevation of temperature, was uncommon, but, on the other hand, the number of instances in which an increased output of acetone bodies accompanied an elevation of temperature was about equal to the number of cases in which patients with an elevation of temperature showed no increased elimination of ketones. There is no measure of the degree of prostration, except the judgment of clinical experience. We were unable to link up in any way the severity of the infection, as indicated by the degree of prostration, with the amount of acetone bodies eliminated in the urine. In Table 1 a few cases are cited to show these conflicting points.

TABLE 1.—ANALYSIS OF DEGREE OF FEVER AND SEVERITY OF INFECTION

Name, Age, Condition	Period	Temperature	Acetone and Diacetic Acid	B-Hydroxybutyric Acid	Food
I. B., 8 yrs. Lobar pneumonia Delirious	1st day	104-106	0.120	0.059	Milk, 200 c.c.; vomited once
	2d day	102-105	0.245	0.124	Milk, 800 c.c. and toast
	3d day	105-98	0.265	0.188	Milk, 200 c.c. and toast
M. L., 9 yrs. Scarlet fever Prostrated	1st day	101-103	0.330	0.333	"Took food well"
	2d day	101-103	0.140	0.016	Milk, 600 c.c.
	3d day	101-103	0.818	0.238	Milk, 560 c.c.
R. F., 15 mos. Bronchopneumonia Extreme prostration	1st day	101-103	0.010	0.013	Took all feedings well throughout period; no vomiting
	2d day	102-104	0.016	0.013	
	3d day	102-104	0.042	0.035	
	4th day	102-103	0.017	0.023	
	5th day	100-101	0.037	0.038	
M. M., 8 yrs. Lobar pneumonia Prostrated	1st day	103-104	0.098	0.108	Milk, 300 c.c.; vomited
	2d day	103-104	0.185	0.197	
E. L., 5 yrs. Scarlet fever Not prostrated	1st day	100	0.306	0.967	Milk, 900 c.c. and bread; no vomiting
	2d day	101-100	0.135	0.082	Milk, bread; ate well
	3d day	100-101	0.140	0.065	Milk, 450 c.c.
S. J., 6 yrs.	1st day	100	0.355	0.688	"Took a little milk"
J. H., 14 mos. Lobar pneumonia Extreme prostration (12 hrs. to death)	1st day	103-105	0.030	0.014	Took food; no vomiting Took no food
	2d day	103-105	0.068	0.007	

INANITION

In a previous paper² we have shown that, as a rule, children show a very moderate increase in the production of acetone bodies as the result of inanition for periods of from twenty-four to forty-eight hours. The cases of infectious disease showing acetonuria usually took food, and, further, the increased acetonuria was in most of the cases out of all proportion to the inanition factor. Although it may not be disregarded entirely, it is by no means possible to explain the acetonuria in the infectious conditions on the basis of inanition.

2. Veeder and Johnston: *Am. J. Dis. Child.* **13**:89, (Jan.) 1917.

UNDETERMINED FACTORS

We were fortunate in obtaining figures on a number of children with cross or secondary infections. That is, determinations were made at the time the patient was admitted with one infection and again later during a second infection developing while the child was in the hospital. Both the absolute number of patients developing acetonuria, and the amount of increased elimination in those showing this acetonuria during the second period was decreased. This is strikingly shown in the cases of C. M. and E. D. (Table 2).

It will be noted that in both these cases the high point occurred during the twenty-four hours immediately after admission. This was true of nearly all of the patients showing acetonuria. In both of these cases the acetone bodies in the second periods did not exceed normal figures. The simplest explanation for this is to assume some psychic factor by which the excitement of moving the patient, bringing him to the hospital, and the new surroundings, produce a reaction not found when the infection develops amid quiet surroundings to which the child is accustomed. It is impossible, of course, to demonstrate the proof of this explanation.

TABLE 2.—SHOWING ELIMINATION OF ACETONE DURING FIRST AND SECOND PERIODS

	Period	Temperature	Acetone	B.
C. M.: Scarlet fever 12 13-13/16	I (2d day of disease)	102-104	0.380	0.650
	II	102-104	0.331	0.488
	III	102-104	0.205	0.118
Measles 2/ 1-2/ 2 1/12-1 15	I	101-103	0.033	0.024
	II	103-105	0.020	0.006
E. D.: Lobar pneumonia	I (4th day of disease)	105	0.140	0.188
	II	105- 99	0.040	0.005
	III	98	0.027	0.006
Scarlet fever 1/15-1/18	I	103-104	0.010	0.000
	II	100-103	0.012	0.000
	III	100-104	0.005	0.004

Our findings do show definitely, however, that while an increased elimination of acetone bodies may occur in the infectious diseases, this does not always take place; that in the same patient it may occur during one infection and not during a second; that it is not dependent on the severity of the infection or the degree of temperature; and lastly that the decreased intake of food, so consistently a part of an infectious process, does not explain the causation.

CLINICAL DEPARTMENT

A REPORT OF TWO CASES OF CONGENITAL STRICTURE OF THE ESOPHAGUS *

JOHN LOVETT MORSE, A.M., M.D.

Professor of Pediatrics, Harvard Medical School

BOSTON

These cases are reported partly because of the rarity of the condition and partly because the symptoms, although very characteristic, are usually misinterpreted and attributed to some other disease.

REPORT OF CASES

CASE 1 (No. 19217).—A boy was admitted to the Children's Hospital when 6 years old. His parents and seven other children were well. One child had died in the Children's Hospital some years before after an operation for esophageal stricture. Further details regarding this case will be given later. The mother had had two miscarriages.

The patient was born at full term after a normal labor and was thought to have been normal at birth. He was breast fed and seemed well in every way until the attempt was made to feed him when he was 1 year old. It was then found that while he was able to take liquids he could not take solid food without vomiting. On this account he was nursed until he was 2½ years old. Since then, he had been able to take liquids and soft solids, but no solid food. Solid food was vomited immediately after it was swallowed. In addition he had spells of vomiting lasting two or three days every two weeks or oftener. These attacks were apparently not dependent on the character of the food. The vomiting had never been projectile. It always occurred immediately after taking food. If he did not vomit then, he did not vomit at all. The vomitus had never contained blood or bile, but was made up solely of food. He never vomited at night. His appetite was poor; his bowels were regular. He had developed normally, creeping at 8 months, walking at 9 months, saying single words at 9 months, and making sentences at 17 months. He had been seen by many physicians, all of whom had made the diagnosis of indigestion and had prescribed various remedies and diets.

He was poorly developed and fairly nourished, weighing 32¼ pounds, and measuring 40 inches in length, while the average for his age is 45 pounds and 42 inches, respectively. He was somewhat pale. He had the characteristic adenoid facies. His teeth were bad, and his lower jaw protruded. D'Espine's sign was negative. There was no dulness under the manubrium or over the spinous processes, and air entered both lungs alike. The rest of the physical examination showed nothing abnormal. The hemoglobin was 55 per cent.; the leukocyte count, 25,000. The tuberculin test was negative, and the urine was normal.

His story in the hospital was the same as it had been outside. He was unable to take solid food without vomiting immediately. At times he took liquids and soft solids without trouble; at other times he vomited them also at once.

Roentgenograms taken after a barium meal showed, according to the report of Dr. Percy Brown, "distinct enlargement of the esophagus at about the level of the sternoclavicular area. The course of the esophagus is likewise well seen below the point of stenosis. From the persistency of the shadow, its cause is believed to be organic rather than spastic." (Figs. 1 and 2.)

* From the medical service of the Children's Hospital, Boston.

Esophagoscopy under ether by Drs. Herman and Pratt showed an obstruction six inches from the incisor teeth which was readily dilated. There was also some constriction at seven inches and onward, more suggestive of congenital narrowing than inflammatory stricture. The stricture was dilated up to a No. 23 bougie, which passed into the stomach with only slight bleeding.

The boy returned a month later for further dilatation. He had gained a pound in weight and had not vomited until about a week before he came back. Dilatation will, of course, have to be continued at intervals.



Fig. 1.—Case 1. Fusiform dilatation of the esophagus at sternoclavicular junction and narrowing below this point. Anteroposterior view.

CASE 2 (No. 5028).—This patient was brought to the hospital seven years ago when he was 25 months old. He is a brother of the other patient. This case was reported by Dr. T. M. Rotch.¹ In brief, he had vomited from four to six times a day ever since birth. The vomiting had always occurred during feeding and had never been forcible. It made no difference whether the food was breast milk, milk or Mellin's food. He often retained several feedings and then vomited two or three in succession.

1. *Am. J. Dis. Child.* 6:1 (July) 1913.

His general physical examination was negative, except that he was thin and pale. A catheter was stopped 15.5 cm. from the incisor teeth. The roentgenogram after a bismuth meal showed a narrowing of the lower one-third of the esophagus with dilatation above. Esophagoscopy by Dr. D. Crosby Greene showed a stricture of the esophagus 17.5 cm. from the incisor teeth. This was approached by a funnel shaped narrowing, after which the esophagus was slightly dilated. The stricture was very small, looking about the size of the lead of a lead pencil. It was deemed inadvisable to attempt to dilate the stricture and a gastrotomy was done. He died a week later.



Fig. 2.—Case 1. Lateral view showing distinctly the enlargement and the constriction below it.

The occurrence of a deformity of this sort in two members of the same family must be most unusual.

CASE 3 (No. 14082).—A girl was admitted to the Children's Hospital when 3 years old. Her parents were well. She was an only child. She was born at full term after a forceps delivery. She was normal at birth and weighed $7\frac{1}{2}$ pounds.

She began to vomit soon after birth. Nursing was given up on this account when she was 2 weeks old. The vomiting, however, continued. It occurred immediately after feeding, never before or at some time after. There were long intervals during which she did not vomit milk or any liquid food. She never failed, however, to vomit immediately whatever solid food was given, even if it was only a small amount. She had been treated by many doctors for the vomiting, but the diets which they had prescribed and the medicines which they had given had never had any effect on the vomiting.

She had done fairly well, however, until six days before she entered the hospital when she began to vomit everything given. She had been unable to retain even water. The bowels had not moved for three or four days, in spite of suppositories. The urine had been scanty and she had probably had a little fever. She was sent into the hospital with the diagnosis of "acidosis," and a question of cardiospasm. The physical examination showed nothing abnormal. The hemoglobin was 76 per cent.; the leukocyte count, 23,600. The tuberculin and Wassermann tests were negative. She weighed 25 pounds.

She was able to swallow without difficulty, but, after taking about $\frac{1}{2}$ ounce, she complained of being sick and then regurgitated without difficulty all the fluid taken. The fluid did not seem to come from the stomach and there was no retching. It was mixed with mucus, but the odor was not acid. The stomach tube was stopped seven inches from the incisor teeth.

Esophagoscopy under ether by Dr. Greene showed that the esophagus was normal to the point of stricture, seven and a half inches from the incisor teeth where there was a small circular opening showing no cicatrix and admitting a No. 7 French bougie. There was no marked dilatation above the stricture. Bougies were passed up to No. 16. She has been dilated repeatedly and now, after eight months, has no symptoms.

PROGRESS IN PEDIATRICS

RECENT WORK IN ANATOMY, PHYSIOLOGY AND PATHOLOGY OF INFANCY AND CHILDHOOD

JAMES B. HOLMES, M.D.

BAETIMORE

ANATOMY

Significance of Striations in Muscle.—Lewis,¹ in some studies on the cells of heart muscle from very young chick embryos, arrives at some conclusions that are of far reaching application. She finds it possible to study with satisfaction the living cells of heart muscle from embryos of ten myotomes. In these cells she finds that complete cross striations are present, and much earlier than has been supposed by other observers. Cross striations are present, but not fibrils. The cross striations are very thin bands on the surface of the cell. They extend across the cell and never appear as narrow threads or fibrils. Fixation of the cell causes the formation of the surface layer into fibrils on which the cross striations are drawn together into deeper bundles, and then become evident as sharply marked structures. In places where the pull on the surfaces of the cell is such that they are not coagulated into fibrils, the cross striations remain spread out as thin bands extending across the cell. No structure resembling the fibrils of the fixed preparation was present in the living heart muscle at any of the ages studied.

"The physiologists have endeavored without success to formulate a theory, based on the myofibrils, to account for the contraction of the muscle cells. It is not surprising that such a theory has not proved satisfactory, at least in regard to the heart muscle, since the structure on which it was based is not a part of the living heart muscle cell, but only of the dead cell. In other words, a cell containing the structure on which it was attempted to build the theory is not capable of undergoing contraction."

The ossification centers of the fetal pelvis receive further consideration from Rosmark.²

R. Taylor³ contributes measurements obtained from 250 full term, newly born infants.

1. Lewis, M. R.: The Development of Cross Striations in the Heart Muscle of the Chick Embryo, *Bull. Johns Hopkins Hosp.* **30**:176, 1919.

2. Rosmark, T.: The Ossification Centers of the Fetal Pelvis, *Am. J. Obst.* **78**:175, 1918.

3. Taylor, R.: Measurements of 250 Full Term New-Born Infants, *Am. J. Dis. Child.* **17**:353 (May) 1919.

Scammon⁴ points out that while accumulated data regarding the growth of gastric capacity have been summarized from time to time in the studies of Pfaundler, Borie, Marfan and Figueira, it is now more than fifteen years since the last attempt at a synthesis of this material. Much valuable new material has accumulated. The material is presented by Scammon in an article that is replete with graphs and references to statistics.

The question of growth of gastric capacity has been approached from many angles, and it is noteworthy that graphic curves based on the data obtained by different methods are of the same general type. Curves of gastric capacity show an initial stage of rapid rise (during the first month of life) followed by a much longer stage in which the rise is slower and without important changes in rate. It is found possible to represent the curves by certain empiric formulas of a single type. In these formulas gastric capacity equals a numerical value plus a multiple of the age of the child expressed in weeks.

PHYSIOLOGY

Metabolism.—Olmstead, Barr and Du Bois⁵ report further studies on the metabolism of growing boys. Two years ago Du Bois reported figures showing that the metabolism in boys 12 years of age is 25 per cent. higher than for an adult of the same height and weight. (As since expressed in other figures by Lusk: The basal metabolism of an average boy, 13 years of age, 4 feet 10 inches in height, and weighing 80 pounds, may be calculated as 1,525 calories a day. This is the same as that of a man, 25 years of age, weighing 126 pounds, and 5 feet 2 inches in height.) It is generally accepted that metabolism is relatively high during childhood, falling rapidly in adolescence, and then decreasing slowly during the rest of life. Du Bois has been fortunate in being able to reexamine certain of the boys whom he had previously studied, some of them now exhibiting signs of puberty. He finds a marked decrease in metabolism, a decrease of 13 per cent. per unit of body surface, for the seven boys studied. The metabolism is, however, still 11 per cent. above the average for adult men between 21 and 40 years of age, and about 4 per cent. above that of adult women.

The Stomach.—F. W. White⁶ has studied the effect of stimuli from the lower bowel on the rate of emptying of the stomach. Studies were

4. Scammon, Richard E.: Some Graphs and Tables Illustrating the Growth of the Human Stomach, *Am. J. Dis. Child.* **17**:395 (June) 1919.

5. Olmstead, W. H., Barr, D. P., and Du Bois, E. F.: Clinical Calorimetry, Paper 27, Metabolism of Boys Twelve and Fourteen Years Old, *Arch. Int. Med.* **21**:621 (May) 1918.

6. White, F. W.: The Effect of Stimuli from the Lower Bowel on the Rate of Emptying of the Stomach, *Am. J. M. Sc.* **156**:184, 1918.

made on men, and, experimentally, on cats. The effects of various irritative lesions were studied. Delay in emptying a barium meal from the stomach was found to be the exception; strong stimuli were needed to slow the stomach. Marked delay in emptying the stomach is far more often the result of actual lesions about the pylorus than of reflexes from the bowel. The stomach emptied itself within the normal time in some cases of ileac stasis of two or more days' duration, and in most cases with good sized twelve hour residue in the ileum, also when the colon was distended with a large enema, also in most cases of chronic appendicitis and chronic inflammations and tumors of the colon. These gastric symptoms in intestinal cases are not, as a rule, the result of slow emptying of the stomach.

Sauer⁷ has utilized thick farina feedings in twelve cases of pyloric stenosis in infants. In all but one case the effect of thick feedings was striking. In eleven of the twelve cases the vomiting soon stopped, although in most of the patients the peristaltic waves and the tumor (where palpable) persisted for weeks or months after vomiting ceased. The infants were seen when from 6 weeks to 2 months of age. The feeding was prepared as follows: One part of farina in seven parts of fluid (three parts of milk to four of water) was boiled in a covered double boiler for one hour. Such a food contains about 15 per cent. of cereal. Salt and sugar may be added. The infants are placed on the right side after feeding, and disturbed as little as possible. Small supplementary fluid feedings are added later.

The Intestine and Drugs.—A. Galvani⁸ considers the administration of epinephrin. He remarks that the soft and elastic arteries in children, and the integrity of the cardiovascular and other systems, render epinephrin peculiarly effective in pediatric practice. He reviews the indications for it, the dosage, etc., as published by various writers. When especially prompt action is necessary, it may be administered subcutaneously, from 0.5 to 1 c.c.; but, except in urgent cases, he advocates administration by mouth, from 10 to 30 drops of the 1:1,000 solution. Its action is more protracted by mouth, and abrupt changes in the circulation are avoided. It is thought to stimulate the centers, possibly by way of the sympathetic system. The effect of the drug on the musculature of the intestines, Galvani notes, is yet undecided. Lesné, in 1912, reported that a given dose of epinephrin injected into the rectum of rabbits caused death, but not so rapidly as when a like dose was injected subcutaneously. The same dose introduced into the stomach or small intestine seemed entirely harmless.

7. Sauer, L. W.: The Use of Thick Farina in the Treatment of Pyloric Stenosis. *Arch. Pediat.* **35**:385, 1918.

8. Galvani, A.: *Rivista di Clinica Pediatrica* **16**:225, 1918.

Binet⁹ in a review of the literature, concludes that epinephrin has an undoubted modifying action on the vascularization, secretion and motor functioning of the digestive tract, and states that digestive disturbances from suprarenal insufficiency are known. Administered by mouth, epinephrin does not seem to display a toxic action; it does not appear to be acted on by pepsin or trypsin or passage through the intestinal capillaries. Administered by rectum, it is powerfully toxic. The writer ascribes this to the close anastomoses between the hemorrhoidal veins and the portal vein, the liver being apparently the barrier which arrests the ingested epinephrin.

Alvarez¹⁰ has studied the action of drugs on different parts of the intestine. Other work convinced him that there are marked differences in the neuromuscular apparatus in different parts of the tract. He made use of segments of rabbit's intestine placed in warm aerated Locke's solution, and tested a great variety of drugs. He found that some drugs stimulated all parts equally; some stimulated in small doses but depressed in large doses; some depressed or stimulated after an opposite initial effect; some acted more powerfully in one part than another; a few actually stimulated one end and depressed the other. Epinephrin stimulated. Mercuric chlorid generally stimulated the colon less than the small intestine.

Dudodenum.—E. G. Grey¹¹ has shown that in the dog it is possible to remove the duodenum, transplanting the major pancreatic duct to the jejunum, and have the animal enjoy comparative good health for at least nine and one-half months, provided the pancreas and the liver continue actively to discharge their secretions into the intestinal tract. He thus refutes the conclusion of Stassoff that the duodenum is essential to life. The operation must be done in several stages, but every trace of the duodenal mucosa and approximately all of the muscular coats can be removed without embarrassing the vascular supply of the pancreas. Withdrawal of the alkaline juices from the duodenum, without removal of the tract, not infrequently leads to the formation of peptic ulcers.

Lactation.—E. L. Cornell¹² reports observations on the effect of placental tissue as a galactagogue. He says that 87 per cent. of the babies whose mothers had received placental tissue began to gain on the fourth and fifth days, against 69 per cent. whose mothers did not

9. Binet, L.: L'Action de l'Adrenaline sur le Tube Gastro-Intestinal, *Presse méd.* **26**:407, 1918.

10. Alvarez, W. C.: Differences in the Action of Drugs on Different Parts of the Bowel, *J. Pharmacol. & Exper. Therap.* **12**:171, 1918.

11. Grey, E. G.: Duodenectomy; Its Effect on the Life of an Animal Transplantation of the Pancreatic Duct, *Surg., Gynec. & Obst.* **28**:36, 1919.

12. Cornell, E. L.: Placental Tissue as a Galactagogue, *Surg., Gynec. & Obst.* **27**:535, 1918.

receive this medication. Forty-four per cent. of the babies regained their birth weight before leaving the hospital, against 24 per cent. who did not.

Milk.—The presence of citric acid as a normal constituent of cow's milk was reported by Soxhlet in 1888. Sommer and Hart¹³ have recently isolated and identified the compound anew. They find that it amounts to approximately 0.2 per cent. of the milk, or 2 per cent. of the milk solids. Citric acid is a recognized constituent of various "acid" fruit juices and vegetables, and to its presence in them some have ascribed their antiscorbutic properties. Sommer and Hart, therefore, studied the effect of heat on the citric acid content of milk. They find that it is not destroyed even by autoclaving the milk; nor are the citric acid salts of milk changed to an insoluble form by heating.

Bosworth and Giblin¹⁴ report the preparation of a considerable quantity of pure casein from human milk. It is found to have the same nitrogen, phosphorus and sulphur content as casein prepared from cow's and goat's milk; it has the same degree of valency and gives the same series of salts with bases; it has the same molecular weight; it is acted on by rennin in the same manner; the paracasein produced by the action of rennin is similar to the paracasein produced by the action of rennin in the casein of cow's milk.

Van Slyke and Baker¹⁵ describe a method of preparing pure casein from milk which is practically quantitative.

Barley.—Steenbock, Kent and Gross¹⁶ present the results of experiments with barley in feeding growing animals. Barley alone does not meet the needs of the growing animal. It contains an abundance of water soluble vitamin, but is deficient in fat-soluble vitamin. The addition of butter-fat improves its growth promoting quality to some extent. Of single additions, a salt mixture, by satisfying the demands of the animal for elements in the group, calcium, chlorin and sodium, exerted the most beneficial effect. Where salts, protein and fat-soluble vitamin were all added, normal growth, reproduction and raising of young became possible.

13. Sommer, H. H., and Hart, E. B.: The Effect of Heat on the Citric Acid Content of Milk. Isolation of Citric Acid from Milk, *J. Biol. Chem.* **35**:313, 1918.

14. Bosworth, A. W., and Giblin, L. A.: The Casein of Human Milk, *J. Biol. Chem.* **35**:115, 1918.

15. Van Slyke, L. L., and Baker, J. C.: The Preparation of Pure Casein, *J. Biol. Chem.* **35**:137, 1918.

16. Steenbock, H. E., Kent, H. E., and Gross, E. G.: The Dietary Qualities of Barley, *J. Biol. Chem.* **35**:61, 1918.

Calcium and Metabolism.—Sherman, Gillette and Pope,¹⁷ and other co-workers, in a series of very careful and prolonged balance experiments, have shown that, in general, an average of 0.45 gm. (about 7 grains) of calcium per adult man per day represents approximately the minimum maintenance requirement for normal nutrition. This amount of calcium is contained in a pint or less of milk; there is less proportionately in meat or common cereals. Though calcium is the most abundant inorganic element in the body, the bones particularly forming a large store of it, nevertheless, as Osborne and Mendel¹⁸ have recently emphasized anew, the supply of calcium cannot long be neglected with impunity in the diet of individuals that have a special need for it, as is true in growth and during gestation and milk production.

The mode of absorption of fats from the alimentary tract has long been a matter of controversy. The present view is that fats are chemically split in the gastro-intestinal tract into fatty acids and glycerols. The fatty acids react readily with bases to form soaps, and as such pass through the intestinal mucosa with varying degrees of facility. The soaps of sodium and potassium are somewhat soluble; those of calcium and magnesium tend to be insoluble. In the case of infants particularly the soaps of calcium are found in the stools. When present in large amounts, or accompanied by other symptoms, the appearance of soap (fatty curds) in the feces has been interpreted as evidence of faulty digestion of fats, or of "fat intolerance," and, as a rule, the amount of fat in the infant's food has been greatly reduced, and often with apparent improvement.

Recently the matter has been approached from a different angle by Bosworth, Bowditch and Gilbin.¹⁹ They note that the calcium content of cow's milk is proportionately higher, compared with the other nutrients, than that of breast milk, a relation which is not altered by merely diluting the milk. This is true also of the phosphoric acid. Both the substances, when fed to infants in the proportions found in cow's milk or in modified cow's milk, are greatly in excess of the amounts supposedly required to supply the demands of the infant, and hence are eliminated either in the urine or in the feces. As the calcium metabolism of bottle fed infants, as measured by the calcium eliminated

17. Sherman, H. C., Gillette, L. H., and Pope, H. M.: Monthly Metabolism of Nitrogen, Phosphorus and Calcium in Healthy Women, *J. Biol. Chem.* **34**:373, 383, 1918.

18. Osborne, T. B., and Mendel, L. B.: The Inorganic Elements in Nutrition, *ibid.* **34**:131, 1918.

19. Bosworth, A. W., Bowditch, L. H., and Gilbin, L. A.: Studies, etc., Calcium in Its Relation to the Absorption of Fatty Acids, *Am. J. Dis. Child.* **15**: 397 (December) 1918.

in the urine, is seldom greater, and often less, than found in breast fed infants, it appears that the excess of calcium must be eliminated in the feces, mostly as insoluble calcium phosphate and calcium soaps, or be ingested at the risk of entering the body fluids and tissues in organic combination and, perhaps, subsequently setting up a toxic condition.

Bosworth, Bowditch and Giblin have, therefore, devised a method by which they reconstruct cow's milk so as to remove much of the calcium. By the use of this reconstructed milk they think they have obtained favorable results in certain cases otherwise difficult to manage dietetically, and in cases classified as "fat intolerance" and "infantile atrophy." Reports of further work by these authors will be awaited with interest.

Meantime, Holt, Courtney and Fales²⁰ have attacked certain of these contentions. They deny that a high calcium intake necessarily causes a serious loss of fat in the feces. Great reduction of the calcium content of the food of infants may, on the other hand, be attended with considerable risk. These authors are of the opinion that it has yet to be demonstrated that infants fed on simple dilutions of cow's milk do not retain an adequate amount of fat, when the stools are formed, or semiformal and soapy. They warn that unless the harm caused by a fairly high calcium intake can be demonstrated quite definitely it would be safer to allow an excess of calcium in the intake rather than to run any risk of providing less calcium than is needed for the normal growth of the bones. The large calcium requirement of children with a tendency to rickets is mentioned; as is also the occurrence of tetany and rickets in children too long fed exclusively on breast milk.

Sato²¹ reports experiments made with the same malt preparation on the same child to determine whether the beneficial effect on the calcium retention attributed to malt extracts is due to the extract itself or to the added alkali. He found that the addition of alkali to milk produced no favorable effect on the retention of calcium, but distinctly an unfavorable one. Malt extract alone appeared to act beneficially on calcium storage. Malt extract to which a considerable amount of alkali has been added seemed to act unfavorably. Thus, if malt soup has a favorable effect on calcium metabolism, it is not as the result of the alkali originally contained in it or added to it.

20. Holt, L. E., Courtney, A. M., and Fales, H. L.: Is the Amount of Calcium Usually Given in Dilutions of Cow's Milk Injurious to Infants? *Am. J. Dis. Child.* **16**:52 (July) 1918.

21. Sato, A.: The Effect of Alkali and Malt Preparations on the Retention of Calcium in Infancy, *Am. J. Dis. Child.* **16**:293 (November) 1918.

Givens²² and McClugage and Mendel²³ have studied two other phases of calcium metabolism experimentally (in dogs). The former, as the result of new experiments, is able to confirm his previous statement that ingested hydrochloric acid is without marked influence on the calcium and magnesium metabolism of the dog. There is an increased urinary elimination of calcium after ingestion of acid, but the absolute amount of this increase is not sufficient to affect to any noticeable degree the calcium balance.

McClugage and Mendel show that, in dogs at least, the calcium in milk is better utilized than that in calcium phosphate, and the calcium in spinach and carrots was poorly assimilated as compared with that in milk.

The outcome of analogous studies in infants, if such are possible, will be of interest. During the past two decades it has become increasingly the practice in infant nutrition to introduce suitable garden vegetables, such as carrots and spinach, into the infant's dietary, and this more especially where the onset of rickets was feared. Recently Courtney, Fales and Bartlett²⁴ presented some analyses showing the effect on these vegetables of the method of cooking employed. It is understood that they are comparatively rich in calcium, and their supposed value has been attributed in part to their effect on mineral metabolism.

Goldschmidt and Dayton²⁵ have studied the effect of sodium, calcium and magnesium salts on the absorption of sodium chlorid in the intestine. They find the colon is not characterized by a strictly one-sided permeability. Toward solution of sodium sulphate it behaves like a semipermeable membrane.

Further work by Bosworth and Bowditch²⁶ bears on the absorption of calcium. They report experiments to show that the ingestion of large amounts of calcium and its absorption as organic salts, if unaccompanied by the ingestion of sufficient phosphorus or chlorin to form soluble salts, may lead to an accumulation of calcium in the tissues, to be followed by a toxic condition and the elimination of

22. Givens, M. H.: Studies in Calcium and Magnesium Metabolism, etc., *J. Biol. Chem.* **35**:241, 1918.

23. McClugage, H. B., and Mendel, L. B.: Experiments on Utilization of Nitrogen, Calcium, and Magnesium, etc., *ibid.* **35**:353, 1918.

24. Courtney, A. M., Fales, H. L., and Bartlett, F. H.: Some Analyses of Vegetables Showing the Effect of the Method of Cooking, *Am. J. Dis. Child.* **14**:34 (July) 1917.

25. Goldschmidt, S., and Dayton, A. B.: The Mechanism of Absorption from the Intestine. I. Colon. One-Sided Permeability of Intestinal Wall to Chlorid, etc., *Am. J. Physiol.* **48**:419, 1919.

26. Bosworth, A. W., and Bowditch, H. L.: Infant Feeding. High Protein Feeding vs. High Calcium Absorption as a Cause of Increase of Body Temperature in Infants, *Am. J. Dis. Child.* **16**:279 (November) 1918.

calcium lactate in the urine. An accompanying high protein content in the food (a synthetic one) they thought responsible only to the extent that it might be a carrier of calcium in the form of calcium caseinate. Once in the body it was thought the calcium might act itself, or as a salt, possibly calcium oxalate.

PATHOLOGY

Of Schoolchildren.—In New Jersey, during the school year 1917-1918, 21,263 children were examined.²⁷ Of this number only 6,243 were reported to be normal, 15,020 were reported to be subnormal, or approximately 75 per cent. of the total number; 4 per cent. were found to be suffering from malnutrition; 5 per cent. from enlarged cervical glands; 15 per cent. with defective vision; 3.5 per cent. with defective nasal breathing; 5.5 per cent. with defective teeth; 8.5 per cent. with enlarged tonsils; 1.25 per cent. with impediment of speech.

As usual, the subnormal children were found to suffer chiefly from defects of vision, from unhealthy conditions of the adenoids and tonsils, and from faulty nutrition. It is obvious that wide latitude must be allowed to individual examiners as to what constitutes an abnormal condition of the adenoids and tonsils.

Malnutrition.—The Dunfermline scale groups children as I, II, III, IV, according to the state of their nutrition, and is based on their appearance only. Holt,²⁸ in a criticism of the figures given out by the New York Department of Health, writes that observations which do not take account of height and weight cannot be relied on as determining the child's nutrition. Figures based on inspection, and made without removing the clothing, cannot be accepted as accurately representing the amount of malnutrition existing among schoolchildren.

Anamniotics.—Massini²⁹ reports the occurrence of an ectromelic monster. The roentgenograms of his case confirm the assumption that the so-called amputations are in reality malformations. The limbs show different malformations above the supposed amputation from constricting bands.

D. M. Greig³⁰ describes an instance of congenital tumor of the frontonasal region. The tumor was pyriform in shape, thick skinned, reddish, 1½ inches in length, and dependent from the region of the l. f. frontonasal suture. It had a translucent appearance, its surface was glazed and smooth, and it was of a somewhat soft consistency.

27. Public Health News (New Jersey), 1918; Abst. J. A. M. A. **72**:1289 (May 3) 1919.

28. Holt, L. Emmett: "Erratum," Arch. Pediat. **35**:512, 1918.

29. Massini, J. C. L.: *Semana méd.* **25**:365, 1918.

30. Greig, D. M.: Two Cases of Unusual Congenital Abnormalities, Edinburgh M. J. **11**:384, 1917.

It could not be diminished by pressure, and there was no evidence that it communicated with the interior of the cranium. A large double hare-lip and cleft palate, more marked on the left side, was also present. The tumor was readily removed under general anesthesia, and was reported to be composed of "fibrous tissue, unstriped muscle, etc."

A. Brown Kelly³¹ describes a teratoid growth on a hairy polypus of the rhinopharynx in a 6-weeks-old female infant. The tongue-like growth was first noticed when the baby was one week old, and had been getting bigger and more troublesome. It was more than 2 inches in length and $\frac{1}{2}$ inch wide in its thickest lower part. It was attached by a slender pedicle to the left side of the rhinopharynx, and frequently protruded from the mouth. The soft, fleshy body was covered with skin, stratified squamous epithelium, provided with numerous fine hairs; the underlying connective tissue was of a loose rudimentary character, with two or three minute glands; the central and larger portion of the polypus was composed of tissue closely resembling fat.

Greig³² reports an instance of congenital Dupuytren's contraction of the fingers. This was observed in a well developed male infant, aged 5 weeks. The mother had noticed since birth a difficulty in getting the child's palms washed, in that she was unable to get the fingers extended. On careful examination under general anesthesia the condition was apparently not a tendinous affection, and there was no evidence of any abnormality in the growth, or peculiarity in the innervation of the muscle. The lesion appeared to involve the skin and the subcutaneous and deep fascia, and to be similar to the condition known as Dupuytren's contraction in adults.

Influenza.—During the recent pandemic of influenza the occurrence of a form of severe croup closely resembling clinically a true diphtheritic croup, but without the presence of the Klebs-Loeffler bacillus, was noted by a number of writers. Coray³³ relates that during the severe wave of influenza at Zurich many children developed laryngeal stenosis, and in one half of his eighteen cases emergency treatment was required. The resemblance to true diphtheria was so deceptive that it seemed antitoxin should be given as a routine measure in such cases, although it probably had no influence on the influenza. Coray was unable to find any mention of croup with influenza in the records of the 1890-1891 epidemic.

31. Kelly, A. Brown: Teratoid Growth on Hairy Polypus of the Nasopharynx, *Brit. J. Child. Dis.* **15**:226, 1918.

32. Greig, D. M.: Two Cases of Unusual Congenital Abnormalities, *Edinburgh M. J.* **11**:384, 1917.

33. Coray: Ueber Kruppartige Affektionen bei Influenza, *Cor.-Bl. f. schwetz. Aerzte* **49**:475, 1919.

Regan³⁴ reports a series of twenty cases, five of which terminated fatally. The bacterial flora found by him was similar to that generally found among influenza cases. There was absence of the Klebs-Loeffler bacillus. The most effective treatment was the use of steam inhalations, followed by intubation, if necessary. The lesion as seen postmortem, is thus described by him:

Microscopic sections of the larynx and trachea show the surface epithelium of the mucosa to be intact, and without presence of fibrin formation, showing thus dissimilarity to diphtheritic laryngitis. The blood vessels of the mucosa and submucosa are seen to be markedly dilated. There is excessive exudation of polymorphonuclear cells, lymphocytes and serum into the surrounding tissues. The thickness of the mucosa and submucosa is greatly increased by this infiltration of tissues and dilatation of blood vessels.

V. B. Philpot³⁵ reports an instance of lymphangioma of the chest in a girl 4 years of age, with complete cure by operation. The child was born with two small tumefactions, one below the axilla and one just above the left clavicle. After a time these began to grow rapidly and the patient became weak and emaciated. The occurrence of abnormally high temperature, from time to time, was supposed to be due to some inflammation in the tumor. At operation it was found that a sac extended below the ribs and formed pockets all through the upper left chest, one of them extending to the scapula behind, and another between the clavicle and the scapula forming the large cyst to be seen above the left clavicle. Drainage, repeated curretting and swabbing effected a complete cure.

Canelli³⁶ has studied the size of the thyroid in infants prematurely born or dying a few days after birth. Assuming that the maximum weight of the normal thyroid is 4.85 gm., he found the thyroid enlarged in four of the seventy cadavers examined. In one instance the thyroid weighed 21.5 gm. No trace of iodine was found in the smallest of the four enlarged thyroids, but the largest one, 0.007015 gm. of iodine was present. A brief historical review of the subject is embodied in the paper.

Brennemann³⁷ reports four additional cases of congenital atresia of the esophagus seen by him since his report of three cases in 1913. In his experience no other congenital anomaly of the intestinal tract has

34. Regan, J. C., and Regan, C.: Influenzal Croup, *Am. J. Dis. Child.* **17**:376 (June) 1919.

35. Philpot, V. B.: A Rare Surgical Case, *South. M. J.* **12**:147, 1919.

36. Canelli, A. F.: Contributo allo studio dello struma tiroideo congenito, *Pediatrics* **27**:264, 1919.

37. Brennemann, Joseph: Congenital Atresia of the Esophagus, with Report of Four Additional Cases, with Three Necropsies, *Am. J. Dis. Child.* **16**:143 (August) 1918.

approximated even remotely such frequent appearance, with the possible exception of hyperplastic stenosis of the pylorus. In all of them the upper end of the esophagus ended blindly, the lower end connecting the stomach with the trachea. There is a striking lack of uniformity in the frequency with which this anomaly is met by pediatricians. Brenemann finds the symptomatology strikingly uniform.

Hymnson and Kahn³⁸ analyzed the intestinal contents (meconium) of five newly born infants. They found the iron and calcium contents similar to those found in hunger feces; the phosphorus was less, the sulphur was much increased. Traces of ammonia were found, but no uric acid. Extremely faint traces of amylose were found, but no trypsin, erepsin, lactase or lipase.

Batchelor³⁹ reports in greater detail the findings in her investigation of the dejecta of seventy-four children with special reference to the isolation of aerobic sporebearers. She found *Bacillus cereus* in thirty-two cases; *B. albolactus* in seventeen cases; *B. pseudotetanus* in nine cases; *B. mesentericus* and *B. subtilis* each in six cases; *B. petasites* and *B. vulgaris* each in two cases.

The normal occurrence of these spore bearing organisms and of yeasts in the intestinal contents is worthy of note, as is also their relation to the bacterial flora of the diet, and their susceptibility to change with changes in the diet,⁴⁰ as shown by Herter and Kendall, Torrey and others.

Lowenburg⁴¹ reports a case of congenital unilocular cyst of the liver (hemangioma) in a male infant 19 months old. These cases are rare; they have been considered by Still (1898), Morris (1913) and Moschowitz (monograph). According to Moschowitz, operative results have been satisfactory. In Lowenburg's case the walls of the cavity were stitched to the abdominal wall, and the cavity was packed with gauze. The walls of the cyst were 1 inch thick, friable, brown, and suggested a membranous lining. The child reacted well after the operation. Later, however, there developed great drainage of serum from the cyst wall, entailing the loss of much water, and mineral and albuminous matter. The child gradually weakened, became asthenic (demineralized) and died.

38. Hymnson, A., and Kahn, M.: Study of the Intestinal Contents of Newly Born Infants, *Am. J. Dis. Child.* **17**:112 (February) 1919.

39. Batchelor, M. D.: Aerobic Spore Bearing Bacteria in the Intestinal Tract of Children, *J. Bacteriol.* **4**:23, 1919.

40. Torrey, J. C.: The Regulation of the Intestinal Flora of Dogs Through Diet, *J. M. Res.* **39**:415, 1919.

41. Lowenburg, H.: Liver (Hemangioma) Congenital Unilocular Cyst of, *Arch. Pediat.* **35**:285, 1918.

Young and Wright⁴² report an instance of congenital defect of the abdominal wall.

Carr⁴³ reports an instance of Hirschsprung's disease, in which secondary calcification of the lower part of the sigmoid and the upper part of the rectum had occurred. The patient, a girl, aged 6 years, was brought to the hospital in a condition of shock and died soon afterward.

Bacigalupo⁴⁴ describes a mucodermoid cyst of the pericardium. He considers that intrathoracic congenital tumors are rare and states that Nandrot⁴⁵ recorded the fifty-seventh case. In certain cases the cyst had extended to and become adherent to the pericardium, but in no case has the cyst involved the pericardium. Bacigalupo's case is believed to be the first case of congenital cyst of the pericardium to be described. The age of the patient is not stated.

Bronson and Sutherland⁴⁶ report an instance of ruptured aortic aneurysm in a child 5 years and 10 months of age. The lesion was a fusiform aneurysm of the secondary arch of the thoracic aorta. The aneurysm apparently followed a partial stenosis of the aorta between the insertion of the ductus arteriosus and the left subclavian artery. That this structure was a congenital anomaly was supported by the presence of a diaphragmatic hernia, subluxation of the joints, and defective cranial development.

The authors give a brief discussion of the etiology of aneurysms in children. From the literature they summarize two instances of aneurysmal dilatation due to partial stenosis of the thoracic aorta,⁴⁷ and also five cases of aneurysm apparently due to congenital anomalies in the structure of the ductus arteriosus; in two of the latter, rupture caused death. In the literature they find seven reports of death following rupture of thoracic aortic aneurysms in children, one case of rupture of the aorta without aneurysm, and two cases of rupture of aneurysms of the abdominal aorta. A roentgenogram and photographs of the specimen accompany the description of their case.

42. Young, W. A., and Wright, E. J.: Congenital Defect of Abdominal Wall, *J. Trop. M.* **21**:158, 1918.

43. Carr, W. L.: Case of Hirschsprung's Disease, *Tr. Am. Pediat. Soc.* **30**:108, 1918.

44. Bacigalupo, Juan: Mucodermoid Cyst of the Pericardium, *J. A. M. A.* **71**:961 (Sept. 21) 1918.

45. Contribution a l'etude des kistes dermoïds du mediastin anterieur, Thèse de Paris, 1917.

46. Bronson, E., and Sutherland, G. A.: Ruptured Aortic Aneurysms in Childhood, with the Report of a Case, *Brit. J. Child. Dis.* **15**:241, 1918.

47. Smith and Targett: Aneurysm of Aorta in a Boy Nine Years Old, *Tr. Path. Soc., Lond.* **48**:53, 1897. Wasastjerna, E.: Fall von Aortaruptur nach Schlittschulaufen, *Ztschr. f. Klin. Med.* **49**:405, 1903.

Rivers⁴⁸ describes an instance of erosion of the blood vessels of the neck in the course of scarlet fever. The patient was 5½ years of age. The symptoms at onset were not characteristic; albuminuria subsequently appeared, and on the twenty-third day after onset a characteristic scarlet fever desquamation was present. At the same time, the child became very ill, and a necrosis of the right tonsil, with a very foul secretion, was found. Two ounces of pus, but no blood, were evacuated from a mass the size of an egg on the right side of the neck. During the night the child was found exsanguinated, lying in a pool of blood. Physiologic sodium chlorid solution was given subcutaneously and a transfusion of mother's blood was done. An attempt was then made to examine the abscess cavity; there was a gush of blood, apparently from the external carotid or the lingual artery. These vessels were ligated and the hemorrhage was controlled. Another transfusion was given and the child improved for two weeks, when there was a second hemorrhage, the result of sloughing of the suture on the external carotid. The child then went on to recovery, though convalescence was complicated by a psychosis.

Howland⁴⁹ reports several cases which ended in death, with marked evidence of circulatory failure, but with no changes other than great cardiac hypertrophy and more or less dilatation. Postmortem the hypertrophy was the striking feature. None of the conditions in which hypertrophy usually occurs were present in any of these cases. The myocardium was normal; the musculature was intact. Howland thinks there is reason for believing that as a result of some nervous or muscular disturbance incoordinate action of the heart results.

Marriott and Howland⁵⁰ report experiments showing that the presence of acid phosphate in the body, even in the absence of renal disease, gives rise to the excretion of urine of a character such as has been previously observed only in nephritic acidosis. It is their opinion that the results of their experiments give additional confirmation to the view that the acidosis occurring in the course of nephritis is due to retention of acid phosphate.

Canelli⁵¹ writes on congenital syphilis of the kidney. He states that this condition is found to be rather frequent at necropsy, being shown by the presence of sclerosis, atrophy, gummas and retention cysts.

48. Rivers, T. M.: Hemorrhage Into a Postscarlatinal Cervical Abscess. Ligation of the Common Carotid. Recovery. *Johns Hopkins Hosp. Bull.* **30**:240, 1919.

49. Howland, John: *Tr. Am. Pediat. Soc.* **30**:2, 1918; abstr. *J. A. M. A.* **71**:221 (July 20) 1918.

50. Marriott, W. McK., and Howland, John: The Influence of Acid Phosphate on the Elimination of Ammonia in the Urine. *Abstr. Bull. Johns Hopkins Hosp.* **29**:264, 1918.

51. Canelli, A. F.: Sifilide renale congenita. *La Pediatria* **26**:257, 1918.

Amyloid degeneration of the kidneys is not characteristic of syphilis in the congenital form. There may be acute interstitial nephritis or a chronic sclerotic (atrophic) form. Tardy inherited syphilis is frequently manifested by a syphilitic albuminuria.

Hinman⁵² reports a cytoscopic study of urologic conditions in children.

Comby⁵³ discusses the occurrence of suprarenal hemorrhage in children. Friderichsen⁵⁴ has shown that the condition presents a uniform and constant symptomatology and is not extremely rare, presenting three cases of his own and twenty-five from the literature. The attack may come on at any age. It occurs suddenly. The child becomes pale or cyanotic, and then quickly moribund, without noteworthy dyspnea or other signs of pulmonary affection. Necropsy always shows the same findings: cutaneous hemorrhages and hemorrhages into the cortex and medulla of both suprarenals. Comby presents three cases, occurring in children 6 months, 10 months and 14 years of age, respectively.

Comby⁵⁵ also presents a case of Addison's disease in a girl 13 years of age. The patient had probably been infected by her father, who had died of pulmonary tuberculosis. She presented all the symptoms of Addison's disease, including bronzing of the skin, profound asthenia, arterial hypotension and vomiting. Death occurred after an illness of about two months. The only lesions found at the necropsy were in the suprarenals. The right gland was converted into an abscess; the left gland was studded with caseous nodules.

Rutelli⁵⁶ describes another case of Addison's disease in a girl, 10 years of age. There was a history of enlarged cervical glands at the age of 10 months, and an affection of one finger which resulted in ankylosis at the age of 2 years. Pigmentation of the skin commenced at the age of 4 years. The blood pressure ranged from 65 to 70 mm., and there was marked asthenia; the urine was normal, except that there was slight diminution in the elimination of urea and creatinin. On a diet rich in carbohydrates, sugar appeared in the urine twenty hours after injection of 1 mg. of epinephrin; on an ordinary diet, after eighteen hours, and on a diet poor in carbohydrates, after four hours.

52. Hinman, F.: Cytoscopic Study of Urological Conditions in Children, *Am. J. Dis. Child.* **17**:306 (May) 1919.

53. Comby, J.: Apoplexie surrenale chez les enfants, *Arch. de méd. d. enf.* **21**:651, 1918.

54. Friderichsen, C.: Hemorrhage in Suprarenals, *Ugesk. f. Læger* **79**:1817, 1917.

55. Comby, J.: Maladie d'Addison chez une fille de treize ans. Mort. Autopsie, *Arch. de méd. des enf.* **20**:28, 1917.

56. Rutelli, G.: Contributo allo studio della matellia di Addison nell'infanzia, *La Pediatra* **24**:274, 1916.

Control experiments in a healthy subject gave similar findings in twelve, eight and two hours, respectively.

Strick⁵⁷ reports a case of congenital absence of the uterus complicated with anomalous vulvovaginal anus. He presents statistical data on the occurrence of the condition.

Comby⁵⁸ discusses the occurrence of abscess of the anus in children. A case seen by him, the patient being 13 months old, recalls to mind an early series of seven cases, and he enumerates the causes of the condition. It usually appears in infants and is rarely tuberculous in origin.

The occurrence of a pouch in the buttocks with an opening into the rectum is reported.⁵⁹

Hayd⁶⁰ reports the occurrence of a small round cell sarcoma in the right ovary of an infant, aged 23 months. It was the size of a goose egg, and was felt in the right lower quadrant as a large, movable, smooth tumor, not painful to the touch. Two or three weeks later the mass had become tender, and considerable fluid was present in the abdomen. On exploration, the tumor was found to be free in the abdomen, with the right tube attached to it. Bloody fluid was present; and on palpating the liver it was found to be much enlarged and filled with nodular masses. The child died several weeks later.

Mandelbaum,⁶¹ in a study of two cases of Gaucher's disease in adults, offers the following conclusions: "Gaucher's disease is characterized by a distinctive, well defined clinical picture and constant, definite changes in the hematopoietic organs. The presence in these organs of peculiar large cells, with a characteristic type of cytoplasm, not duplicated in any other disease, is a distinguishing histologic feature. These cells are derived from the reticular apparatus of the hematopoietic structures, but an additional origin from the endothelial cells of the venous sinuses of the spleen cannot be denied. Fat or lipid bodies cannot be found in the large cells by microchemical or polariscopic tests. The peculiar substance in the large cells does not lie in the extractive group, on chemical analysis, but is apparently of complex protein nature, in combination with lipoids. The disease is evidently caused by some disturbance of metabolism, the products being found in a specific group of cells (reticulo-endothelial) of the hematopoietic system."

57. Strick, E. J.: A Case of Congenital Absence of the Uterus with Anomalous Vulvovaginal Anus, *Am. J. M. Sc.* **156**:75, 1918.

58. Comby, J.: Absces a l'anus chez les jeunes enfants, *Arch. de med de enf.* **21**:365, 1918.

59. Pouch in Buttocks Opening Into Rectum, *Arch. Espanola de Pediat.* **2**:533, 1918.

60. Hayd, H. E.: Sarcoma in the Left Ovary in a Child Twenty-Three Months Old, *Am. J. Obst.* **78**:764, 1918.

61. Mandelbaum, F. S.: Two Cases of Gaucher's Disease in Adults. A Study of the Histopathology, Biology and Chemical Findings, *Am. J. M. Sc.* **157**:388, 1919.

Carr and Moorhead⁶² report a case of Gaucher type of splenomegaly.

Inaba and Ohashi⁶³ report the finding of a new microbody in the blood in a case of myelogenous leukemia.

Jemma⁶⁴ reports a case of malignant lymphogranuloma in a girl, 6 years old. The disease had existed for ten months. The tumors were situated chiefly in the cervical region. There was intermittent fever and increasing pallor and weakness. The von Pirquet test was positive. The blood examination showed 53 per cent. lymphocytes—in a total count of 7,600 leukocytes—and tubercle bacilli. Scattered Schrön-Much granules were found in material taken from the glands.

Ward⁶⁵ discusses the nature of von Jaksch's disease.

Schwarz⁶⁶ discusses the occurrence of a chlorotic type of anemia in infants and children.

Wolbach and Morse⁶⁷ report a case of neuroblastoma sympaticum, and Humbort and Naville⁶⁸ report a case of neurofibromatosis.

Barron⁶⁹ reviews the subject of meningitis in the newly born and in early infancy. He refers to Koplik's recent paper⁷⁰ and tabulates forty-two cases reported in the literature since 1895, when Sherer appears to have reported the first cases. The causative organisms in these cases were, in order of frequency: *B. coli*, fourteen cases; staphylococcus and streptococcus, six cases; meningococcus cases, five; streptococcus, four cases; pneumococcus, 4 cases; tuberculosis, three cases, and *B. lactis-acrogenes*, *B. pyocyaneus*, *B. mucosus-capsulatus*, *B. typhosus*, *B. influenzae*, *B. catarrhalis*, one case each. In Barron's case—a male infant, born in breech presentation in which the delivery was assisted by inserting a finger into the mouth and then exerting a moderate amount of traction, and which died from meningitis on the eleventh day—the causative organism was definitely *B. coli-communis*.

62. Carr, J. G., and Moorhead, L. D.: Report of a Case of Gaucher Type of Splenomegaly, *J. A. M. A.* **72**:19 (Jan. 4) 1919.

63. Inaba, Ttsuyoshi, and Ohashi, Shin: A New Microbody Found in the Blood in a Case of Myelogenous Leukemia, etc., *Am. J. Dis. Child.* **16**:1 (July) 1918.

64. Jemma, R.: Sul linfogranuloma maligno, *Pediatrics* **26**:513, 1918.

65. Ward, G.: Nature of von Jaksch's Disease, *Brit. J. Child. Dis.* **15**:101, 1918.

66. Schwarz, Herman: The Chlorotic Type of Anemia in Infants and Children, *Arch. Pediat.* **35**:430, 1918.

67. Wolbach, S. B., and Morse, J. L.: Neuroblastoma Sympaticum, *Am. J. Dis. Child.* **16**:63 (July) 1918.

68. Humbort, G., and Naville, F.: Neurofibromatosis, *Ann. de méd., Par.* **5**:108, 1918.

69. Barron, Moses: Meningitis in the New-Born and in Early Infancy, *Am. J. M. Sc.* **156**:358, 1918.

70. Koplik, H.: Meningitis of the New-Born and in Infants Under Three Months of Age, *Arch. Pediat.* **33**:481, 1916.

Barron tabulates also the probable portal of entry in nineteen of the forty-two cases. The figures are as follows: spina bifida, four cases; otitis media, four cases; hematogenous, three cases; eustachian tube, one case; mouth, one case (Barron's case); lungs, umbilicus, intestine, circumcision wound and placenta, each one case. Meningitis in the new-born and in early infancy is a rare disease.

It appears that *B. coli* occupies in the meningitis of early infancy the important place held by *B. tuberculosis* in the later months of infant's life. The pathogenic strains of *B. coli* may show marked variations in form, in rates of fermentation and in motility. Most of the strains isolated in the cases tabulated by Barron were actively motile. The avenues of infection in the new-born, in general, have not been definitely established. La Fetra⁷¹ believes that infants are born septic very rarely. Scherer, Noeggerath and Hermann believe that contaminated water of the bath tub is a frequent source of infection. According to Scherer, infected liquor amnii furnishes a similar possibility. Aschoff,⁷² in the course of careful studies, found that the passage of liquor amnii up the eustachian tubes during premature respiration is fairly common; he believed that resulting inflammation occurred not from infection thus introduced, but only from the fluid acting as a foreign body, a locus minoris resistentiae being caused. Bonhoff and Esch⁷² held that infection occurred in this manner in their case. Rasch^{72a} believes that infection of the external auditory canal is more important than infection of the eustachian tube. Others believe that the umbilicus is the most important route. The possibility of injury of the mucous membrane of the mouth by the accoucheur's finger giving a portal of entry has been suggested. Barron thinks this occurred in his case. Infection through the intestinal tract is possible.

The susceptibility of infants to infection with organisms that are otherwise only slightly pathogenic may be explained, concludes Barron, by the feebleness of antibody production during the early months of infancy (Halban and Landsteiner); and the greater resistance of breast fed infants over artificially fed ones is probably due to the compensation of the passive immunization by the breast milk for the active immunization which is still deficient.

71. La Fetra, L. E.: Accidents and Diseases of Early Weeks, Arch. Pediat **33**:401, 1916.

72. Bonhoff and Esch: Ueber einen Fall von Meningitis purulenta beim Neugeborenen, infolge rechtseitiger Mittelohrentzündung, Ztschr. f. Geburtsh. u. Gynäk. **70**:886, 1912. Cited from Barron.

72a. Rasch: Ueber die Häufigkeit und Bedeutung von Mittelohrentzündung bei Kleinen Kranken Kindern, Jahrb. f. Kinderh. **37**:319, 1844. Cited by Barron.

Kramer and Wright⁷³ report an instance of meningitis due to *Streptococcus pyogenes-hemolyticus* in a mother and her unborn child. The fetus was 40 cm. long. The authors believe that this occurrence supports Rosenow's dictum of elective localization in the maternal and fetal meninges.

Hunt⁷⁴ reports a case of juvenile paralysis agitans.

Naville⁷⁵ reports the microscopic findings in a typical case of amaurotic family idiocy. The infant was the fourth in a family of six children to be thus affected. Naville describes aplasia of the tracts in addition to the usual lesions of this form of idiocy. Clinically, he recognizes a juvenile form and atypical forms, besides the usual infantile form. All are believed to proceed from the same pathognomonic degeneration of the cells. The eye findings may vary widely. A connection with certain other familial diseases of evolution is suggested, essential atrophy of the optic nerve, Marie's cerebellar ataxia, etc., and certain mendelian features are pointed out.

Talbot⁷⁶ reports studies on the energy metabolism of an amaurotic family idiot.

28 East Mount Vernon Place.

73. Kramer, G. B., and Wright, W. B., Jr.: Streptococcic Meningitis in the Mother and Child in Utero; Report of a Case, *J. A. M. A.* **71**:729 (Aug. 31) 1918.

74. Hunt, J. R.: Case of Juvenile Paralysis Agitans, Primary Atrophy of Pallidal System of Corpus Striatum, *Neurol. Bull.* **1**:237, 1918.

75. Naville: Pathological Anatomy of Amaurotic Familial Idiocy, *Arch. f. Neurol. u. Psychiat.* **1**:286, 1917.

76. Talbot, Fritz B.: Energy Metabolism of an Amaurotic Family Idiot, *Am. J. Dis. Child.* **16**:39 (July) 1918.

The American Medical Association will pay thirty cents each for the following issues of the AMERICAN JOURNAL OF DISEASES OF CHILDREN: January, 1913; February, March, November and December, 1914; January and August, 1915; January, 1918; March and April, 1919. Address to AMERICAN MEDICAL ASSOCIATION, 535 North Dearborn Street, Chicago, Ill.

American Journal of Diseases of Children

VOL. 19

MARCH, 1920

No. 3

DILATATION OF THE COLON IN CHILDREN *

ALFRED EDWARD MEYERS, M.D.

SAN FRANCISCO

In reviewing the literature that has appeared on the subject of dilatation of the colon in children one is struck by the lack of definiteness pertaining to this condition. The various theories put forth endeavoring to point out the etiology of this abnormality are but a frank admission of our uncertainty. Likewise, the medical treatment of intestinal dilatation with its accompanying constipation is highly unsatisfactory, both to the parents of the patient and to the physician.

In the first place, What degree of hypertrophy and dilatation constitutes the so-called Hirschsprung's disease, otherwise known as congenital idiopathic dilatation of the colon, or megacolon? If one makes roentgenograms in all cases of persistent constipation, especially those beginning in infancy, he would find that many of the sigmoids are looped, twisted, redundant, dilated and hypertrophied. The past histories of these cases are practically identical. In spite of rational feeding during the early part of infancy, a bowel movement without the aid of a suppository, enema or laxative was a rare occurrence. Distention with gas was a noticeable feature, always causing abdominal protuberance. Normal growth was usually interfered with, and the patients were always below par. All seemed to fall an easy prey to the infectious diseases, thus manifesting an evident lowering of their resistance. But constipation was the dominant symptom which compelled them to seek medical advice. Lubricants such as paraffin oil, laxatives such as milk of magnesia or phenolphthalein, cathartics such as castor oil, and enemas of salt solution and oil were given daily with the hope that the bowel would sooner or later function normally, but the relief was only temporary, and the final result very unsatisfactory.

Correcting the diet received but very little attention, a factor very essential in combating the gaseous distention accompanying this condition. In 80 per cent. of the cases of chronic intestinal indigestion

*From the Department of Pediatrics, University of California Medical School.

one will find, on analyzing the diet, that the carbohydrates greatly predominate. The following diet is typical of that received by these patients:

Breakfast: Cereal, milk, toast, sometimes an egg.

Dinner: Meat (occasionally), vegetables (of all sorts), potatoes (in nearly every dietary), rice, spaghetti or macaroni. Desserts: puddings (tapioca or corn starch).

Supper: Soup, bread, milk or tea, cooked fruit or cake.

A glance will show that this dietary is unbalanced, and that the starchy elements make up nearly 80 per cent. of the food.

Regularity of habit is frequently tried, but the mother soon exhausts her patience in endeavoring to make the child try to move its bowels without the aid of some external stimulus, and the only encouragement she receives is that as the child grows older the intestines will take on their normal function. It is quite true that in a certain percentage of these cases, their little bodies grow up to meet this abnormality, but, as in many other conditions, Nature exacts her usual penalty.

Holt¹ gives the following as his interpretation of Hirschsprung's disease, or megacolon: "It is characterized by a great increase in the diameter of the colon and in the thickness of its wall. It was originally believed to be an idiopathic condition for which no sufficient anatomic cause could be found. Hence, it has been known as congenital or idiopathic dilatation of the colon." This seems to coincide with the views of most observers. From the same source the following definition of hypertrophic stenosis of the pylorus, with reference to its pathology, is taken: "The pathology of stenosis of the pylorus in early infancy is somewhat obscure and quite diverse views are held. It is believed by some that the primary and essential condition is one of spasm; that the hypertrophy, when it is present, is secondary; and that in many of the cases there is pylorospasm without hypertrophy.

The other view, and that which seems to harmonize best with the clinical symptoms and the pathologic findings, is that the primary condition is one of hypertrophy which is congenital; that spasm is added to this; that in all cases both factors — hypertrophy and spasm — are present; that while the cases differ in degree, they are the same in kind. Spasm certainly plays an important part in the production of symptoms; but to regard this condition as one essentially of muscular spasm seems to us erroneous." Thus we see that in the former condition (megacolon) there is hypertrophy (colon) and dilatation (sigmoid), and in the latter (pyloric stenosis) hypertrophy (pylorus) and dilata-

1. Holt, L. Emmett, and Howland, John: *Diseases of Infancy and Childhood*, Ed. 7, New York, D. Appleton & Co., 1918, pp. 321 and 408.

tion (stomach). Histologically, in congenital dilatation of the colon, the mucosa is twice its normal depth, contains pigment masses (chronic inflammation), while the muscularis mucosa is hypertrophied, especially in the region of the circular fibers. The microscopic picture of pyloric stenosis is very similar in that the circular muscle fibers are hypertrophied.

Enemas are essential in the treatment of megacolon, and attention is given to stimulating peristalsis by laxatives and cathartics as well as to correcting the diet. In hypertrophy of the pylorus, the dilated portion (stomach) is subjected to lavage, careful attention is given to the diet, and in many cases, especially where spasm is present, atropin is given with very good results. Dilatation of the colon does harm by predisposing to malnutrition, intestinal disturbances and intercurrent infections, while pyloric stenosis blocks the passage of the food into the system. Both conditions are treated medically and surgically with equally good results. The following table lists the symptoms as they appear in both conditions:

	Dilatation of the Colon	Pyloric Stenosis
Hypertrophy	Present	Present
Hypertrophy of circular muscle.....	"	"
Dilatation	"	"
Visible peristalsis	"	"
Constipation	"	"
Congenital malformation	"	"
Gastro-intestinal retention	"	"
Spasm	?	"

If, as has been shown, there is a similarity between megacolon and hypertrophic stenosis of the pylorus, and if, as is well known, there are different degrees of the latter, varying all the way from an occasional slight spasm, manifested by the vomiting of a few cubic centimeters of food, to the very severe type in which there is hypertrophy and spasm combined and wherein it is impossible for the child to retain even boiled water in the stomach, why is it not possible for all the dilated, elongated and redundant colons which we see in constipated children to constitute varying degrees of megacolon? It seems to me that it would help to clarify an obscure point in a condition not definitely understood if we could eliminate the term "Hirschsprung's disease" and classify all cases according to the amount of dilatation, slight, moderate, or great, as the case might be, the latter to embrace what is known as megacolon, and the former all those conditions showing from a slight to a moderate amount of redundancy.

In the second place, What is the true cause or exciting factors of dilatation of the colon? Perhaps the best classification of the various theories advanced is that given by Barrington-Ward:² (1) Mechanical; (2) neuropathic; (3) dilatation following colitis, and (4) congenital anomaly.

2. Barrington-Ward, L. E.: Brit. J. Surg. 1:345, 1914.

Many cases of dilated colons have been reported wherein the cause of the trouble was traced to a mechanical obstruction, but the fact that this condition has been reported in a premature child, that postmortems show no obstruction in many cases, and that constipation begins in the first weeks of infancy, seems sufficient proof against the theory of mechanical obstruction.

Walker and Griffith³ advanced the idea that dilatation of the colon might be due to distention by gas following an attack by colitis. The same arguments as against the mechanical idea may be applied to this theory. It is true that the mucosa in megacolon shows evidence of chronic inflammation and very often the feces are covered with mucus, but both may be the result instead of the cause. It is easily conceivable that an unrecognized case of dilatation of the colon of a slight degree may be complicated with a colitis, which in turn favors the transition to one of greater degree. It is also possible that a colitis may be caused by fermentation usually present in a dilated colon.

The concensus of opinion seems to be that dilatation of the colon is a congenital abnormality in the lower end of the hind gut, which takes the form of a muscular hyperplasia. It usually involves the rectum and spreads a varying distance up the colon. The abnormality may affect one or all segments of the intestines. Thickening of the walls and increase in the lumen are caused by the hyperplasia of the muscle fibers. Considerable clinical and pathological evidence has been presented since Hirschsprung⁴ gave his classical description supporting this view, but my experience with a case of megacolon and five other cases of partial dilatation, diagnosed from the history, clinical symptoms and roentgenogram of all the colons, leads me to believe that there is still another element concerned in this condition, that of spasm.

REPORT OF CASES

CASE 1 (49630).—Mother and father are living and well. One brother, aged 7 years, is living and well. No children dead. No miscarriages. Mother's uncle was insane. No history of cancer, rheumatism or nervous diseases. Parents are receiving no treatment for any condition.

Past History.—Child was born in Nova Scotia. Delivery normal. Birth weight 7 pounds. Breast fed for nine months, when child was weaned and fed on Nestlé's food, cow's milk and pap. Present diet consists of cereal, turnips and other vegetables, potato and fruit. Meat was rarely given. With the exception of the present condition, patient has always been well. No operations or accidents. Sat up when 6 months of age; first teeth at 4 months; walked at 13 months; talked at 15 months. Always subject to croup.

Present Illness.—Constipation began as soon as the child was put on cow's milk and other food. Bowels moved regularly while on breast milk. Would go four days without defecation, if permitted, though mother usually gave an

3. Walker and Griffiths: *Brit. M. J.* **2**:230, 1893.

4. Hirschsprung: *Jahrb. f. Kinderh.* **32**:1, 1888.

enema at the end of forty-eight hours. Child seemed lazy and would not try to make its bowels move, even though mother tried in various ways to persuade him. Passed considerable gas and always had a prominent abdomen. Did not seem quite as active as other children. Appetite very good and slept well.

Physical Examination.—Well developed and well nourished male child, 4 years of age. Eyes showed slight conjunctival redness, otherwise negative. Nose normal. Teeth, gums and throat normal. Glands not palpable. Thymus and thyroid negative. Heart showed no enlargement or irregularity or murmurs, and sounds were of good force and intensity. The second pulmonic



Fig. 1.—Showing marked improvement in case of megacolon after treatment. Note difference in size of lumen of colon.

sound was accentuated. The lungs were negative to auscultation and percussion. The abdomen was moderately distended. No masses, free fluid or tenderness present. Liver and spleen not enlarged. Skin rather pale. Muscles flabby and of poor tone. Reflexes normal. Genitals negative. Rectum negative. Urine was negative for albumin, sugar, acetone and diacetic acid. There was a slight trace of indican present. The sediment was negative. The stool was mushy in character, foul and remnants of food were present. Microscopically, many granules were present. The von Pirquet reaction was negative. The

Wassermann reaction was negative. The child was given a bismuth enema and a roentgenogram of the colon was made. The diagnosis submitted by the roentgen-ray department was: megacolon—large redundant sigmoid.

The patient was put on the following starch-free diet: (The juice of one orange one-half hour before breakfast):

Breakfast: Well done, lean, crisp bacon; one soft boiled egg; 8 to 10 ounces of milk.

Dinner: Chop, fish, chicken or scraped beef; 2 to 4 tablespoons of junket; 2 to 4 tablespoons of custard; 8 to 10 ounces of milk.

3 p. m.: Glass of milk or 2 or 3 ounces of ice cream.



Fig. 2.—Showing a redundant and looped sigmoid in a case of persistent constipation.

Supper: 2 to 4 tablespoons of cottage cheese; 2 to 4 tablespoons of gelatin; 8 to 10 ounces of milk.

(Total number of calories in the above diet, about 1,400.)

In addition to the above diet, the child was given 5 drops of atropin sulphate solution, each drop containing $\frac{1}{4,000}$ grain, three times daily. This was increased one drop daily.

Subsequent History.—In two weeks, mother reported a decided improvement in the constipation, by which time the child was receiving 10 drops of the atropin solution, three times daily. Vegetables and fruit were gradually added to the diet and the atropin solution was reduced. The following note was

recorded March 19: "Condition very good. Only twice in two weeks did mother have to resort to enema. Advised to decrease atropin."

April 3, the mother reported that the child had a normal movement every other day, though large; yesterday had three movements normally. Now getting 6 drops, three times a day. Weight, 17.6 kilos (slight increase). April 10 a second roentgenogram was taken, this showing a decided decrease in the size of the lumen of the colon. Constipation again set in because of the impaction of the bismuth in the rectum. The atropin was again instituted until the bowels began to function normally and daily. July 8, the mother reported that the child had had a normal movement daily for two months, and that she believed that her child was cured. A third roentgenogram was taken, and the decrease in size of the lumen was so noticeable that the roentgen-ray department returned the plate with simply "redundant sigmoid" as the diagnosis.

Comment.—Here is a case of dilatation of the colon (megacolon) diagnosed both clinically and with the aid of the roentgen ray. Constipation dates from infancy and has been persistent. All sorts of drugs were tried, but no attention was given to the preponderance of starch in the diet. Assuming that spasm was playing a rôle in this condition the child was put on increasing dosages of atropin, starting from five drops of a 1/1,000 solution until the child complained of dryness of the mouth. Gradually, well done toast, cooked fruit and green vegetables were added to the diet and the atropin was decreased. The constipation ceased after the spasm was relieved and normal defecation followed.

CASE 2 (52933).—Father living and well. Mother living and suffers from bronchial asthma. No other children. None dead. No miscarriages. No tuberculosis, cancer, rheumatism or nervous diseases in the family.

Past History.—Child was born at full term and delivery was normal. Birth weight, 8 pounds. Breast fed for eight months. Sat up at 8 months, first tooth at 6 months; walked at 16 months; talked at 18 months. Children's diseases: Measles at 3 years of age. Later had "kidney trouble" and was sick for two weeks. Eyes were swollen. No symptoms since except occasional scalding of the urine. No enuresis, but child gets up to pass urine during the night. Appetite fair. Sleep is restless.

Present Illness.—Constipation since six weeks of age, since which time child has never had a normal movement of the bowels. Various cathartics and enemas were constantly given. Child was never allowed to go longer than thirty-six hours without a movement. Passes considerable gas and abdomen always prominent.

Physical Examination.—Well developed and nourished girl 4 years of age. With the exception of slightly hypertrophied and cryptic tonsils and a very prominent abdomen, the physical examination was negative. Weight, 35 pounds; height, 41 inches. Urine negative for albumin, sugar, acetone and diacetic acid. Examination of stool showed a moderate amount of undigested starch; was foul, mushy and showed some evidence of fermentation. A roentgenogram of the colon showed a redundant and looped sigmoid (Fig. 2).

Treatment.—The child was put on a starch-free diet and given 5 drops of the atropin solution as above, to be increased one drop daily. Fruit juices were allowed both morning and night to offset the constipation usually present with a starch-free diet.

Subsequent History.—The constipation did not improve until the child was receiving 9 drops of atropin solution three times daily. Cooked fruits and vege-

tables were added to the diet, and the atropin solution decreased. After three months the mother reported that the child was having a normal bowel movement every day, having discontinued the atropin several weeks before, and was now on a mixed diet.

CASE 3 (51246).—Father and mother living and well. One brother living and well. One miscarriage (spontaneous). No tuberculosis, rheumatism or nervous diseases.

Past History.—Child was born at full term and delivery was normal. Was breast fed for one year, then given a general diet. First tooth erupted at six months. Walked and talked fairly early. Children's diseases: scarlet fever, "summer complaint," pneumonia. Appetite always good. Bowels always constipated. Gets colds easily.



Fig. 3.—Showing slight redundancy of sigmoid, and moderate dilatation of rectum in a case of persistent constipation.

Present Illness.—During the last two years has had frequent attacks of high fever accompanied with a cough. Bowels have been constipated since child was 2 months of age, and would only move when cathartics and enemas were given. Mother has never allowed the child to go longer than forty-eight hours without a bowel movement. Stools are usually hard.

Physical Examination.—Well developed and well nourished boy 6 years of age. With the exception of a rather pendulous abdomen, somewhat distended, and an acute phimosis, the physical examination was negative. The von Pirquet reaction was slightly positive. The urine was negative for albumin, sugar, acetone and diacetic acid. Examination of the stool showed it to be mushy in character, foul and not well formed. Microscopically, there was a moderate amount of undigested starch. The child was given a bismuth enema and a roentgenogram was taken of the colon. This showed a moderate amount of redundancy of the sigmoid and a very large rectum.

Treatment and Subsequent History.—The child was put on a rigid starch-free diet for a few days. Fruit juices were allowed. Atropin sulphate solution was given, starting with 5 drops, three times daily. Improvement was noted one week after treatment was instituted. Additions were made to the diet, and after two weeks the atropin solution was discontinued. The last notation on the history was as follows: "Doing exceedingly well and bowels move normally every day. Child is given raw and cooked fruit, such as peaches, pears, apples, apricots and plums. Appetite is very good. Diet contains only a slight amount of starch."



Fig. 4.—Showing redundancy of sigmoid extending up to transverse colon. Figures 1 and 6 are of the same case.

CASE 4 (30465).—Father living and well. Mother living, suffers from headaches. No tuberculosis or exposure. No history of rheumatism, cancer or nervous diseases. No miscarriages.

Past History.—Child was born at full term after a rather difficult labor. Because of sickness following immediately after delivery, mother was unable to nurse it. Was fed on cow's milk for one month, then changed to Eagle Brand condensed milk which it was fed for one year. Early digestion was fairly good. Sat up at 6 months of age, walked at 13 months and talked at 15 months. Children's diseases: Croup at 1 year of age, which has persisted

off and on up to the present time. At 3 years of age child began to have vomiting spells, lasting for four or five days. It was projectile in character and usually associated with constipation. Is never without a cold or cough of some sort. In 1917, patient contracted scarlet fever; temperature 104 F. Urine always negative. Following this infection child has always been constipated and has been compelled to use cathartics and enemas. Has considerable gas.

Present Illness.—About once a month patient has a vomiting spell which lasts from one to four days. Bowels are always constipated and cathartics are used to keep the bowels free. In the interim the child seems to be in fairly good health and comfortable. There is some pain connected with the vomiting.

Physical Examination.—Well developed and nourished child, 9 years of age. Seems to be of a nervous temperament. Parietal bosses very prominent. Eyes and nose negative. The teeth are in good shape. The tonsils and adenoids are hypertrophied. The posterior glands are palpable. The heart and lungs are negative. The abdomen is very prominent, but no masses, fluid or tenderness present. Liver and spleen are negative. The child had an acute phimosis, and circumcision was advised to be done when the tonsils and adenoids were removed. (This physical examination was made two years ago.)

Treatment and Subsequent History.—The vomiting spells and constipation have persisted up to the time of child's visit to the clinic in August, 1919. The physical examination at this time was as follows: Child somewhat undernourished; middle right turbinate enlarged; teeth irregular; tongue coated and papillae very prominent; tabs of tonsillar tissue in fossae; submaxillary and cervical glands are palpable; apex of heart 8 cm. to the left of mid-sternal line, in the fourth space, there is a soft systolic murmur at the apex, not transmitted; the second pulmonic is greater than the second aortic; abdomen is negative; skin is dermatographic; reflexes normal. Pulse 96; pressure 85 (systolic), and 65 (diastolic). The blood showed nothing abnormal. Examination of the stool showed considerable free starch. The urine was negative for albumin, sugar, acetone and diacetic acid. The child was given a bismuth enema and the colon was screened. (Through a misunderstanding no roentgenogram was taken.) The roentgen-ray report was as follows: "Moderate redundancy of sigmoid; moderate dilatation of rectum." A complete gastro-intestinal series was made a few days later. After six hours, one half the bismuth remained in the stomach, with the head of the barium column in the colon. The spleen was enlarged. The splenic flexure was distended with gas. The pyloric sphincter was thickened. Conclusion: Constipation and splenomegaly; marked gastric stasis unexplained except by thickened pylorus. The child was put on a starch-free diet and given the atropin solution as above. In two weeks the mother reported the condition much improved. Toast and baked apple were added to the diet. Two weeks later the child continued to improve. The last note on the history was as follows: "Child's improvement quite noticeable. Has had no vomiting attacks. Bowels move every day, the amount being small the first day but quite large the following day. Appetite and sleep very good. Vegetables allowed. Has had no vomiting attacks for two and one-half months. Advised mother to continue with the atropin solution because of the pylorospasm."

CASE 5 (54305).—Father and mother living and well. One brother living—has stomach trouble. No children dead. No miscarriages. No tuberculosis, rheumatism or nervous diseases in the family.

Past History.—Child was born at full term and delivery was normal. Breast fed. At 1 month of age had a slight intestinal upset, since which time child has always been constipated. Sat up at 8 months; first tooth erupted at 8 months; walked at 13 months. Has never had any of the infectious diseases. Tonsils and adenoids were removed one year ago.

Present Illness.—Persistent constipation since infancy. Mother has tried various measures for relief, but the child is unable to move its bowels without the aid of a cathartic or enema. Has always been more or less under par.

Physical Examination.—Well developed and well nourished child, 5 years of age. With the exception of a very prominent abdomen, the physical examination was negative. The urine was negative for albumin, sugar, acetone and diacetic acid. Examination of the stool showed considerable undigested starch. Roentgenogram of the sigmoid showed redundancy of the sigmoid and dilatation of the rectum.



Fig. 5.—Showing redundancy of sigmoid and dilatation of rectum in a case of persistent constipation.

Subsequent History.—This patient was put on a starch-free diet and the atropin solution. The result of the treatment in this case is not known, as the patient did not return to the clinic, and it seemed impossible to get in touch with them.

CASE 6 (33048).—Father living (is sick—cause unknown). Mother living and well. No other children living. None dead. No miscarriages.

Past History.—Child was born at full term and delivery was normal. Birth weight, 7½ pounds. Breast fed for three months. Early digestion seemed good, but child was always constipated. Had measles at 2 years of age. Later had varicella. Has frequent colds.

Present Illness.—Constipation since child was a baby. Mother has tried massage over the sigmoid, as well as cathartics and enemas, but condition has not improved. Appetite is variable. Mother thinks child's abdomen is more prominent than normal. Does not seem to have any desire to move its bowels. Diet is an unbalanced one and contains a great deal of starchy food. Stools are usually hard.



Fig. 6.—Showing remains of barium meal six hours after feeding—partial pyloric stenosis and hypertrophy in a child 10 years old. Patient had periodic attacks of vomiting. Roentgen ray of colon showed dilatation of sigmoid.

Physical Examination.—Fairly well developed and nourished female child aged 4½ years. With the exception of hypertrophied tonsils and adenoids, the physical examination was negative. The urine showed a very slight trace of albumin, orthostatic in character; it was otherwise negative. The stool showed an excess of undigested starch, and was foul and mushy. The Wassermann and von Pirquet reactions were negative. The roentgen-ray showed redundant sigmoid extending up to transverse colon.

Subsequent History.—The child was put on a starch free diet and given increasing dosages of the atropin solution, beginning with 5 drops, three times daily. Improvement did not begin until the child was taking 27 drops daily. Vegetables were added to the diet and the atropin was reduced. Two months after treatment was instituted the mother reported as follows: "Condition very good. Bowels move daily and normally. No drops for the last two weeks. Appetite much improved." Urine is negative for albumin. Child has gained one pound in weight.

The child having moved when the roentgenogram was being taken, caused the negative to be blurred just enough to make it unfit for clear reproduction, and therefore has been omitted.

DISCUSSION

From an analysis of the above cases it would seem that all those patients treated were helped materially, and any procedure which helps a patient with a dilated and nonfunctioning colon to have a normal

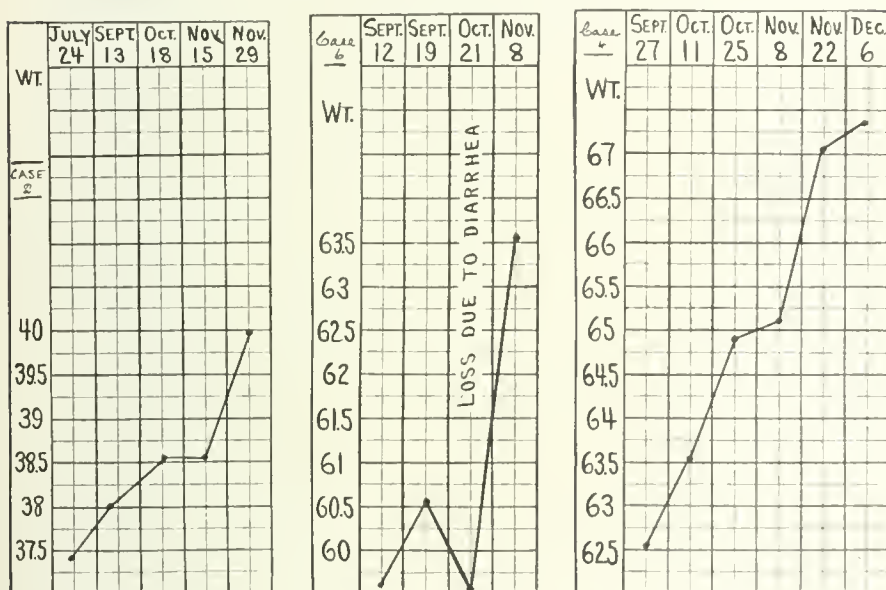


Fig. 7.—Weight curves of three infants following change of diet.

bowel movement every day is worth while. Too often we are confronted by these little ones who have been constipated since birth, and we cheer the mother along by telling her that the child will outgrow the condition, while at the present time she must go ahead with her lubricants, enemas and laxatives. It is also interesting to note that the constipation did not cease until atropin was given. This, I feel, was due to the action of the drug on the smooth muscle fibers of the intestines which were in a state of spasm. Furthermore, after the bowels began to function normally the atropin was stopped and the constipation did not return.

CONCLUSIONS

In conclusion, I would suggest that more roentgenograms of the colon be taken in cases of persistent constipation, especially those dating from infancy. In eight consecutive cases the lower bowel was found to be abnormal and the cause of the condition ascertained. We will at least know more about the etiology even if we cannot help them all medically.

OSTEOGENESIS IMPERFECTA CONGENITA *

H. M. McCLANAHAN, M.D., AND W. W. WILLARD, Ph.G.

OMAHA

This condition was first described by Vorlik in 1849. Up to 1906, 140 cases had been reported. So many names have been used in the description of bone abnormalities in infants that an uncertainty remains as to just what is meant in some of these descriptions. For example, Lovett and Nichols,¹ after a careful study of all the case reports, conclude that only fourteen of these are true cases of osteogenesis imperfecta congenita. Since the introduction of the roentgen ray the descriptions have been more accurate. Valuable articles on the subject have also recently been contributed by Schwartz and Bass,² Griffith,³ Hess,⁴ Bookman⁵ and Mixsell.⁶

Two types are recognized, namely: osteogenesis imperfecta congenita and osteogenesis imperfecta tarda. Authors are convinced that there is a clearly defined distinction between these two types. It is a rare systemic disease of unknown etiology, characterized by imperfect development of bone, numerous fractures and excessive callus formation.

The condition has been described in textbooks under a variety of names as follows: Osteomalacia congenita; rachitis foetalis annularis; malacia myeloplastica; periosteal dysplasia; dystrophia periostale; osteitis parenchymatosa chronica; micromelia annularis; osteoporosis congenita; fragilitas ossium.

Some authors (Griffith,³ Schwartz and Bass⁴) uphold the theory of an hereditary tendency; others, however, find no familial influences. A study of the recent literature would indicate that syphilis is not a cause. There is no evidence of a disturbance of the endocrine glands, and environment is not a factor.

Opinion differs as to the process of bone formation in this condition. Axhausen says that there is a deficiency in periosteal bone formation due to the lowered function of the osteoblasts, but that the preparatory calcification of cartilage and the absorption of bone are normal. According to Sigowa, the pathologic process consists in a

* Read before the American Pediatric Society, June, 1919

1. Lovett and Nichols: Brit. M. J. **2**:915, 1906.

2. Schwartz and Bass: Am. J. Dis. Child. **5**:131 (Feb.) 1913.

3. Griffith: Am. J. M. Sc. **113**: 1897.

4. Hess: Arch. Int. Med. **19**:163 (Feb.) 1917.

5. Bookman: Am. J. Dis. Child. **7**:436 (June) 1914

6. Mixsell: Arch. Pediat. **34**:756 (Oct.) 1917.

disproportion in the building up and breaking down leading to osteoporosis. Whatever the theory, the fact is that bone formation from periosteum remains in a primary fibrous state. Osteoporosis is a secondary result from the excessive formation of medullary spaces, due to deficient development of bony substance and increased absorption. In the congenital type of case, such as the one described, a more remote cause is embryonal failure of the periosteum and endosteum at the time when ossification should begin, so that the lime salts are deposited in small amounts.

The study of the bone in this case shows evidence that the osteoblasts rising from vascular fibrous bone marrow, because of insufficient nourishment or some toxic influence, did not develop properly, but remained polygonal and later underwent metaplasia into osteoclasts.

REPORT OF CASE

Baby L., male, was admitted to University of Nebraska Hospital, Oct. 1, 1918, aged 3 months. Breast fed up to the time of admission.

History.—Parents in good health. Two older children living and well. No miscarriages. Pregnancy normal and full term. Labor normal. Deformity was apparent at birth. Infant had several fractures, including forearm, thighs and legs. Masses in shafts of long bones easily felt. Head was large and soft. Cry had always been feeble; nursed readily; bowels regular and of yellow color; urine free.

Condition on Admission.—The infant lay on a cot, with thighs flexed on body, seldom moving unless disturbed. The cutaneous reflexes were normal. The abdomen was large, with an umbilical hernia. Spleen and liver were normal. Arms and legs were bent and deformed. Masses of callus could be palpated in the shafts of the humeri, femora and tibiae. Ribs felt soft and pliable, with no discernible fractures. Head felt like a membranous bag with small islands of bone here and there. The skin was soft; the eyes followed objects; no exophthalmos. Heart and lungs were normal; weight 7 pounds and 2 ounces. The mother was certain that the baby had grown, but it was not weighed at birth. Wassermann was negative; von Pirquet tuberculin test was negative. Urine: specific gravity, 1.008; albumin, negative, diacetic acid, negative; acetone, negative; indican, positive; microscopic examination negative.

Blood: Hemoglobin, 70 per cent.; red blood cells, 3,640,000; leukocytes, 18,700. Differential leukocyte count: polymorphonuclears, 56 per cent.; lymphocytes, 40 per cent.; eosinophils, 2 per cent.; special forms, 2 per cent.

As the mother did not remain with the infant, it was placed on a modified milk mixture. The child remained in the hospital from Oct. 1 to Nov. 16, 1918. During the first two weeks of its stay it made a gain of 10 ounces in weight; the next two weeks it lost 8 ounces, due to indigestion and withdrawal of food. For the next three weeks it lost 4 ounces. During the last three days of life, while acutely ill it lost 17 ounces of weight. Ten days before death there developed numerous small furuncles over the body. A culture of the pus revealed *Staphylococcus aureus* in pure culture. While in the hospital, the temperature varied between 99 and 102 F. The bowels were normal, except on two occasions. The urine was free and did not stain. He constantly remained very quiet. The arms were placed in light splints at right angles to the body; the legs were constantly flexed. No attempt was made to apply splints to the legs. November 14, he developed a temperature of 105.6 F. with cough and dyspnea. Respirations were from 60 to 90. The temperature ranged from 103 to 105 F. during entire period of sickness. Examination of

the chest revealed fine râles over the posterior chest with small areas of dullness on percussion. During the last twenty-four hours of life there were frequent attacks of cyanosis, and for the last twelve hours of life there was a constant expiratory grunt. Death from exhaustion, November 18, with a loss in weight of 17 ounces, during this period. As far as can be ascertained from the literature, this is the youngest case with a fatal issue which has been reported in which a careful histologic study has been made.

The conclusions of Professor Willard agree very closely with those recorded by Nichols on an infant dying at the age of 10 months, the youngest previously reported.

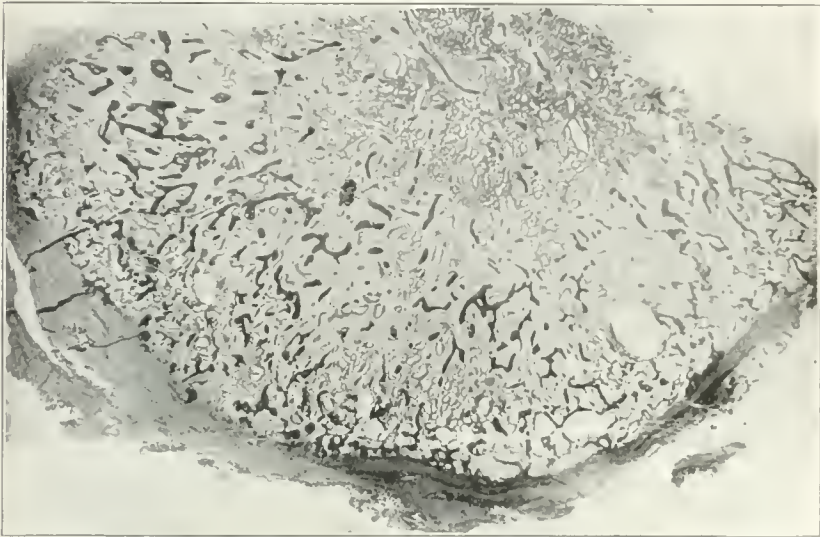


Fig. 1.—Half of transverse section of diaphysis of left femur. Decalcified in nitric acid and formol. Doubly embedded in celloiden and paraffin. Section cut 10 microns thick. Stained in hematoxylin and eosin. Photomicrograph shows an enlargement of 10 diameters. The partially ossified trabeculae are shown black. They are less numerous near the center of the shaft and extend slightly into the periosteum at the periphery. The periosteum is much thicker than normal. It reacts to fracture of the bone by still further thickening, as indicated on the left side of the section. Note the absence of a wall of compact subperiosteal bone which in the normal would extend half way to the center of the diaphysis although the total diameter of the normal is less than half that represented in this case. The blood sinuses of the marrow are the numerous smaller open spaces. Blood cells are adherent to their endothelial walls showing as a darker border to the spaces. The larger spaces in the periphery are possibly shrinkage spaces in the mucoid-like marrow. Blood forming marrow cells are abundant only in the center of the bone where they give a darker appearance to the section.

The apparent shortening and bending of the legs are believed to be due to the pull of the muscles. The relative shortening of the legs and the long body would suggest achondroplasia. However, in the latter condition there is interference with the proliferation of ear

tilaginous cells in the zone between the shaft and epiphysis, resulting in shortening and premature ossification of the long bones. There is also a premature ossification of the sphenoid and the sphenoidal processes of the occipital bone which lead to skull clavis. Both of these conditions are absent, as shown by the roentgenogram and the microscopic studies of the epiphyses. The thickening of the bone is due to increased deposition of cartilaginous cells.

The soft condition of the bone, the multiple fractures and the excessive callus formation combine to make the diagnosis of osteogenesis imperfecta congenita.

REPORT ON NECROPSY

A postmortem examination was made five hours after death by Dr. J. A. Wineberg.

Inspection: Small furuncles were scattered discretely over the head, trunk and extremities. The face was that of an "old man"; the body was emaciated; weight, 5 pounds 15 ounces; the head was large, easily compressed; the arms and legs were short and curved. Callus masses were readily palpated.

Abdomen: No gross changes noted in intestines, liver, spleen or kidneys. No excess of free fluid.

Chest: Both lungs show patches of consolidation with small areas of hemorrhagic infarctions on section. Pleura shows no adhesions. Thymus and thyroid normal. Suprarenals normal. Brain not examined.

Bones: Long bones show multiple fractures with false joints in right tibia and left humerus. Periosteum not ruptured, except on the humerus and on the tibia. On removal of the bones, the left humerus was broken in being dissected out. The bones have a grayish appearance; are easily bent; are soft and pliable. A number of callus rings were present on the site of former fractures.

Microscopic Examination.—The spleen shows congestion. Large areas of necrotic tissue are present in the lungs similar to other postmortem findings in influenzal pneumonia. Kidneys show parenchymatous degeneration. Liver, thyroid, thymus and suprarenals normal. The histologic examination of the bone was made by Dr. Willard.

As the name indicates, this case is one of imperfect development of bone. The interest in the histologic side of the question centers chiefly in the attempt to discover in what way the normal process has been arrested or diverted. This is not easy to do in the absence of stages in the process, the normal of which is an extremely complex and imperfectly understood subject.

However, the outstanding features of normal bone development are well known, involving as they do the early development of an embryonic cartilaginous skeleton which in fetal life is largely replaced by bone and to which are added other bones developed in fibrous tissue and known embryologically as membrane bones.

The histologic structure of all bone tissue is the same regardless of origin, owing to the fact that it is always formed by accretion or deposit of osseous matrix through the combined activity of certain cells derived from embryonic connective tissue. It is thus formed

locally wherever these osteoblasts are active, and when once formed, is fixed, unless absorbed. Such absorption or destruction of bone is a normal part of bone growth and is supposed to be accomplished by large multinucleate cells known as osteoclasts. If this is true, the form and architecture of a bone depends on the balanced interplay of osteoblasts and osteoclasts. The cause behind this is unknown, and must be answered before a real explanation of osteogenesis imperfecta can be advanced.

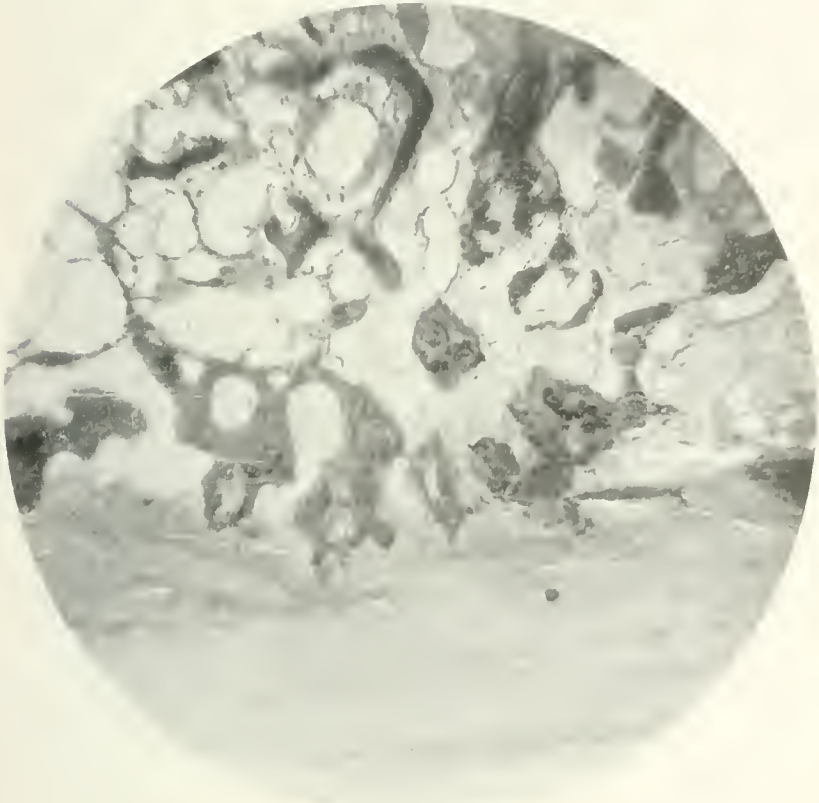


Fig. 2.—Detail from Figure 1. Magnification, 50 diameters. The full thickness of the periosteum with some adjacent bony trabeculae are shown. The darker central areas of the trabeculae are cartilage which has been formed from the periosteum.

Previous investigations on osteogenesis imperfecta indicate that all the bones of the body show much the same changes. We may, then, take the features presented by sections of the femur as typical of this condition. The sections shown in Figures 1, 2 and 3 are from the middle of the shaft or diaphysis of the bone, but they can only be fully understood through a consideration of the bone as a whole. First,

consider the condition of a normal long bone in the new-born child. The shaft is slender but composed of an outer shell of compact bone, which in the case of the humerus is one fourth the total diameter. The marrow cavity is traversed by strong trabeculae entirely of bone. The cartilage of embryonic days has long since been absorbed and no new cartilage is formed. The epiphysis, on the other hand, is composed entirely of hyalin cartilage. The ossification centers that will appear later are preceded at this stage by a vascularization. The region where



Fig. 3.—Small portion of the field shown in Figure 2. Magnification, 100 diameters. This shows the transformation of periosteal tissue into trabeculae. The encapsulated cartilage cells shown at the left represent the first stage in this process.

the cartilage abuts on the marrow cavity of the shaft is the zone of cartilage absorption and spongy bone formation. As long as the bone is capable of growing in length this zone persists. The increase in length depending directly on a process of cartilage formation in this zone between the epiphysis and the shaft of the bone. Keeping pace

with this cartilage formation on the side of the epiphysis, cartilage absorption is going on next the marrow cavity. This absorption is incomplete in that slender remnants are left which offer the scaffolding on which the osteoblasts of the marrow begin the deposit of bone, thus building up bony trabeculae and contributing the necessary strength to the shaft until the sides of the shaft shall have been strengthened through the formation of a wall of compact bone laid down underneath the periosteum. With the normal growth at the ends of the bone but with the absence of periosteal bone formation at the sides, there would be formed a shaft consisting of a fibrous periosteum enclosing marrow tissue through which anastomosing bony trabeculae would run. If the actual formation of bony tissue around the trabeculae should be still further reduced, they would consist of little more than cartilage remnants with one or two lamellae of bone tissue covering them. If, along with this reduced activity on the part of the osteoblasts or bone forming cells there exists increased or even normal activity on the part of the osteoclasts or bone absorbing cells, there is nothing left in the process to result in bone of any strength whatever.

REPORT OF HISTOLOGIC EXAMINATION OF BONE

A study of the sections in this case of osteogenesis imperfecta shows evidence that the normal processes of bone growth have been diverted in all these ways. All accounts seem to agree that cartilage is formed in the normal way and that the vacuolization of the cartilage leading to the formation of the primary marrow spaces in ossification centers occurs normally but that this process is not met by an immediate and active formation of bony tissue on the part of the osteoblasts. The cartilaginous epiphyses are normal in size and character in this specimen, but the section through the diaphysis as shown in Figure 1 shows complete absence of periosteal bone formation. The periosteum is abnormally thick but there is no bony wall underlying it. The trabeculae scattered through the marrow are slender, and section shows them to be poor in bone tissue. They all show cartilage remnants indicating that bone development has not gone beyond the initial stage. On the other hand, the actual size of the shaft is three times that of normal. Comparison shows that a normal humerus of a new-born child has a slender shaft about 5 mm. in diameter with an enlarged epiphysis of 15 mm. In this case, the shaft of the humerus has a diameter of 14 mm. while the epiphyses corresponds to that of the normal at birth. It should further be stated, that the normal shows a marrow cavity of less than 3 mm. surrounded by a wall of compact bone more than 1 mm. in thickness. The thick stocky form of the bones in osteogenesis imperfecta may be explained as the result of muscle pull on a shaft that has no supporting walls, but histologic study of the periosteum indicates that there is also a process of transformation of subperiosteal tissue into certain constituents of the marrow. This would contribute to the process that widens the marrow cavity. This subperiosteal zone is the one region where abnormal process seems to be an active one. The osteogenic layer of the periosteum, instead of forming orderly circumferential layers of bone, expresses itself in this abnormal condition through the formation of poorly developed type of cartilage. This arises in localized areas and pushing out into the marrow cavity form trabeculae which may become slightly bony as in the case of the other trabeculae. One may recognize in Figures 2 and 3 showing detail of this

region groups of encapsulated cells resembling embryonic cartilage. Between the bases of these trabeculae which extend in from the periosteum multinucleate cell masses often appear. These have the structure of osteoclasts and transitional forms trace their origin to the deeper cell layer of the periosteum. Similar masses are smaller and less numerous throughout the rest of the marrow.

The marrow and its vascularization is strikingly different from the normal. The delicate reticular tissue of normal marrow is replaced by a mucoid-like ground substance containing relatively few cells. Many of these being large fibroblasts, giving tissue a distinctly embryonic appearance. Throughout the marrow are large sinusoidal blood vessels with distinct endothelial lining. The characteristic marrow cells of blood-forming function were found in abundance only in the central part of the section. Careful analysis of these cells could not be made from the material thus far studied, but typical myelocytes, nucleated red cells and megakaryocytes (giant marrow cells) were prominent.

In the foregoing general account there has been no attempt to discuss the literature bearing on the microscopic study of the bones in cases of osteogenesis imperfecta. This will be left to a later study of the cellular elements. This case, as far as presented, agrees in essentials with the description by Michel and others.

CHONDRODYSPLASIA: MULTIPLE CARTILAGINOUS EXOSTOSES

REPORT OF CASES *

HUGH L. DWYER, M.D.

KANSAS CITY, MO.

Until a comparatively recent time, the disease characterized by the formation of multiple cartilaginous exostoses was thought to be a rare affection. Gibney¹ reported the first case in this country in 1875, and in the following year recorded the occurrence of the disease in several members of a family. In 1917, Ehrenfried² reported twelve cases and reviewed the literature on the subject. He found that only twenty-nine cases had been reported in America up to that time, and that about forty-two additional cases were mentioned in the discussions. This report stimulated interest in the subject, and case reports during the past two years have been more numerous.

In the cases described, all degrees of associated distortions and deformities of the skeleton are depicted, from the occurrence of simple multiple bony growths causing no particular disturbance, to the occurrence of marked deformities, shortening of the limbs, dwarfing, and associated neurologic symptoms of such severity as to incapacitate the individual. Boggs³ describes a case of multiple osteochondromata, with great deformity, muscular dystrophy and involvement of the cranial nerves, with blindness.

Ehrenfried found that about 5 per cent. of the reported cases were complicated by malignant osteocartilaginous tumors.

The majority of the cases reported occurred in the period of adolescence and young adult life. A few cases have been reported in children, and Hess in discussing Cowie's⁴ paper, refers to an affected family in which the youngest patient was 2 years of age.

* For permission to study these cases I am indebted to Dr. Roger H. Dornett, Director of the Pediatric Clinic, New York Postgraduate Hospital.

1. Gibney, V. P.: Multiple Exostoses, *Med. Rec.* **10**:300, 1875.

2. Ehrenfried, Albert: Hereditary Deforming Chondrodysplasia, Multiple Cartilaginous Exostoses, *J. A. M. A.* **68**:502, (Feb. 17) 1917.

3. Boggs, T. R.: Multiple Congenital Osteochondromata with Degeneration of the Cranial Nerves, and Muscular Dystrophy, *Bull. Johns Hopkins Hosp.* **24**:310, 1913.

4. Trans. American Pediatric Society, 1917. Abstr. in *J. A. M. A.* **68**:235, (July 21) 1917.

Three members of a family came to my attention in the outpatient department of the New York Postgraduate Hospital. Two children were brought to the hospital—one a girl, aged 7 years, with a small bony growth on the front of each leg immediately below the knee, and on each arm immediately below the shoulder joint, and a boy, aged 20 months, with a growth on the left scapula. Suspecting the nature of these growths, inquiry was made regarding similar growths in other members of the family, and it was learned that the father was affected, but that the mother and the other daughter, 5 years of age, were not affected.

REPORT OF CASES

CASE 1.—Tina S., white female, aged 7 years, was born in America, of Italian parents.

Family History.—Mother and father are living and well. They are short in stature, but not a disproportionate shortness. The mother has no visible or palpable abnormalities. The father has bony growths on the legs.

Personal History.—Birth was normal. She was breast fed for seventeen months. The first tooth erupted at 6 months; she sat alone at 7 months and walked at 10½ months. She had measles early in life and pertussis at 6 years.

Present Illness.—When the patient was 3 years of age, hard growths appeared on the front of both legs, about four inches below the knees, and on the front of both arms immediately below the shoulder joints. These protuberances grew out rapidly for a short time; but apparently stopped growing a few months later. They caused no trouble and were not painful.

Physical Examination.—On the medial surface of the upper third of the right humerus, a slight enlargement could be seen. Palpation revealed a spur of bony consistency, not tender, and over which the soft parts were freely movable. The spur pointed downward, so that the finger could be hooked under it; it seemed to be about one inch in length and the globular shaped head indicated that it was pedunculated. On the left humerus, in the corresponding area, a smaller bony mass could be palpated. Two growths of the same consistency and about one or one-half inch in diameter were felt on the medial surfaces of both tibiae, immediately below the tuberosities. Small growths could be felt on both radii, just above the styloid processes, on the clavicles, and several suggestive, though not distinct, enlargements were noted on the phalanges of both hands.

The patient was well developed and well nourished; the head was well shaped and there was no disproportionate shortness of the limbs. The circumference of the head was 19½ inches, and of the chest 21 inches; the height was 43½ inches, and the length of the legs, from the anterior iliac spine to the internal malleolus, was 23½ inches. The middle of the body fell at a point 1½ inches below the umbilicus.

The parents were not aware of any growths, except those on the tibiae and the right humerus. They were causing no trouble whatever and the patient was brought to the hospital only because the protuberance on the arm was noticeable enough to excite comment from those who saw the child.

CASE 2.—Boy, aged 20 months; born in America; a brother of the preceding patient.

Personal History.—Birth was normal; breast fed for nineteen months; he had intestinal disturbances with vomiting and diarrhea early in life, and pertussis when 9 months of age. His first tooth erupted at 6 months; he sat alone at 8 months and walked at 13 months of age.

Present Illness.—A bony enlargement on the back, behind the right shoulder, was noticed when the patient was 5 months of age. It grew out rather rapidly for a few months, then stopped.

Physical Examination.—A mass of bony consistency, about $1\frac{1}{2}$ inches in diameter, could be felt on the right scapula, inferior to the spine. On the third digit of the little finger another growth could be felt. No other protuberances



Fig. 1 (Case 1). Cartilaginous growths on tibiae and femurs.

could be palpated along the accessible parts of the skeleton. The patient was well developed and presented no other abnormalities. The head measured 20 inches, and the chest 19 inches in circumference. The length of the body was $31\frac{1}{2}$ inches, and the middle point was at the umbilicus. The length of the arms was $12\frac{1}{2}$ inches, and the legs $15\frac{1}{2}$ inches.

CASE 3.—John S., aged 29 years; born in Italy; father of the two preceding patients.

Family History.—His mother is dead. Father and one half brother live in Italy, and two sisters live in America. To the best of his knowledge, no other members of his family have abnormal bony growths.

Physical Examination.—The patient is $5\frac{1}{2}$ feet in height, is well developed and there seems to be no disproportion between body and limbs. A bony mass can be felt on both tibiae just below the tuberosities.

The only remaining child, a girl, aged 5 years, was submitted to a physical and roentgenologic examination, and was found to be unaffected.

Roentgen-Ray Examination.—Radiographic examination by Dr. William H. Meyer showed multiple osteochondromata on the various long bones, near the epiphyseal lines. The involvement was bilateral in nearly every instance, and the symmetry was marked, although the size of the growths on either side varied considerably in some instances. The bones principally involved were the tibiae, the radii, humeri, femora, clavicles and scapulae. The pelvic bones, the metacarpals and the phalanges were involved to a lesser extent.



Fig. 2 (Case 1).—Spur on left humerus showing the "blown out" lamellar structure.

The part of the bone chiefly involved was in the region of the epiphyseal line, the shaft being comparatively free. There was none of the shortening, curving, and marked thickening of the long bones with globular bubble-like vacuolation at the ends, as was found in the cases described by Ehrenfried. The roentgen ray appearance of the large growths is that of a blown out cystic formation in the lamellar structure, which connects with the lamellae of the shaft but does not extend up into the shaft for any great distance. The small growths appear as clean-cut exostoses, the defect in the shadow indicating that they are composed of cartilage and bone. The larger growths tend toward spur formation, the spur always pointing away from the nearest joint, a phenomena that seems to be characteristic of this disease.

The most prominent growths on the children were removed and studied microscopically by Dr. Meeker.

PATHOLOGIC REPORT

CASE 1.—Tina S. Nature of specimen: Eechondrosis.

Gross: Specimen, measuring $18 \times 10 \times 10$ mm., presents a rounded surface showing cancellous bone.

Microscopic: One border of the specimen consists of cartilage with scattered cells in a clear ground substance. Inside this the bone is irregularly deposited with spaces between the trabeculae. A thickened periosteum extends



Fig. 3 (Case 1).—Pedunculated growth on right humerus

along the sides of the bone, which is most irregular in outline. The picture is typical of the usual growths on bones of children sometimes associated with rickets.

Diagnosis (Fetal) Eechondrosis, not yet eechondroma

CASE 2.—William S.

Gross: Two pieces, measuring $17 \times 15 \times 16$ mm. and $13 \times 10 \times 20$ mm., respectively. Both are bony in consistency, smooth on one side, which is covered by cartilage, and a cut surface showing cancellous bone.

Microscopic: The picture is the same as the sister's specimen. There is the same irregular atypical change from cartilage to bone, the irregular thickened periosteum with irregular bone outline and deposits of cartilage in the periosteum, all atypical of this form of growth.

Diagnosis: Fetal eechondrosis, not a true tumor

The terms *ecchondrosis* and *ecchondroma* or *chondroma* are usually used to define cartilaginous new growths. The former is confined to those simple hypertrophies of preexisting cartilage and the latter to cartilaginous growths in any part of the body. The occurrence of these growths, in the cases described, away from the epiphyses, and on the shaft of the bone and on other bones where cartilage does not exist normally, and the microscopic appearance of deposits of cartilage in the



Fig. 4 (Case 1).—Cartilaginous spur on upper end of right tibia and femur.

periosteum, is evidence that the condition is one of *chondrodysplasia*, rather than a simple hypertrophy, and the term *ecchondrosis* is not suitable because of its limitations. *Ecchondroma* indicates a benign cartilaginous growth anywhere in the body, and fits well with the condition here described.

The term suggested by Ehrenfried, hereditary deforming chondrodysplasia, is not applicable at present to these cases, because there is no deformity, but when we take the ages of these children into consideration, we must recognize the possibility of some deformity later in life, inasmuch as the disease is an anomaly of skeletal growth, and it is probable that the condition is still active and will be until skeletal maturity is attained.

Some of the deformities usually found in these patients are shortness of stature, which is practically constant, even to the extent of



Fig. 5 (Case 1).—Cartilaginous spur on upper end of left tibia and flat growth on femur.

dwarfing, the lack of growth being in the legs, not the trunk, short upper limbs, relative shortening of the ulna and bowing of the radius causing the hand to deviate outward.

The account of Case 4 was obtained from the records of the Children's Mercy Hospital in Kansas City, where the patient was admitted in the service of Dr. C. B. Francisco.

Case 4.—C. J., white, male, born in Missouri, July 4, 1907.

Family History.—Father died of tuberculosis; two sisters and two brothers dead, cause not stated. The mother is living and well and has had one miscarriage. One sister, living and well, has no bony growths, but the two living brothers have had growths removed from the limbs.

Personal History.—Dec. 2, 1913, he entered the hospital with a deformity of the left arm and a growth under the great toe which caused him to walk on the side of the foot. He was operated on and a large exuberant growth was removed from the ventral surface of the great metatarsal bone. Exostoses were also removed from the anterior and posterior surface of the head of the left radius. Jan. 6, 1919, he reentered the hospital with the statement that the small growths noticed in infancy had steadily increased in size. He had many exostoses, the most prominent were those on the upper ends of both tibiae, the right external malleolus, and in the left popliteal space. A growth two thirds the size of a lemon was removed from the popliteal space, and one the size of a walnut from the inner side of the femur.

The Wassermann test was positive.

Injury to blood vessels, such as trauma, and aneurysm, due to friction from bony growths, have been reported, especially injuries to the popliteal artery.

The neurologic manifestations noted are ulnar and radial nerve involvement, cord lesions from endostoses, and in one case acromegalic symptoms from a growth in the sella turcica.

NATIONALITY

The nationality of the patients collected by Ehrenfried shows that these cases occurred more often among the Dutch and the Germans, and only once each in an Austrian, a Canadian, an Englishman and an Italian. Two cases occurred in the negro, and Cox's patient is a native of India.

HEREDITY

The heredity feature is well established, and Ehrenfried states that the condition can be transmitted by an unaffected mother, but there is no evidence that the disease can be transmitted by an unaffected male. In the cases reported since Ehrenfried's review, I have been able to find support for this statement. In Cowie's patient, the disease was transmitted by the affected father. In Hess's three patients, the disease was transmitted by the affected father, and in Gorsaline's five cases, a man inherited the condition from the father, and, in turn, transmitted it to two children by his first wife, and five children by his second wife.

Gorsaline mentions a case in a man who has a sister, herself unaffected, but with an affected daughter, thus proving that the unaffected mother can transmit the disease.

5. Gorsaline, C. S.: Familial Deforming Chondrodysplasia Multiple Cartilaginous Exostoses, *Am. J. Roentgenol.* **6**:271 (June) 1917.

SEX INCIDENCE

Reineke, in 1891, found that the sex incidence was 3 to 1 in favor of the male, and Ehrenfried, in 1917, found it to be about 5 to 2. Since that time I find that in twenty-nine cases, including my own, the males were affected eighteen times and the females eleven times, a ratio of about 3 to 2.

When we attempt to find an explanation for the high incidence among males, and the transmission of the disease by supposedly unaf-



Fig. 6 (Case 3).—Cartilaginous growths on tibia and fibula

ected females, it would seem that the affection, if mild, would be more readily discernible on the male body and certainly the male would not be so reluctant to make known the condition and present himself for examination. The wider use of the roentgen ray may bring many more cases to light that would otherwise have escaped attention in the days when most of these cases were reported, and the incidence between the sexes may be more equal. However, this is merely speculative, although there is some evidence of it, in the case reports of the past two years.

AGE

All ages have been mentioned in the case reports from the 2 year old patient of Hess to Frieburg's 80 year old man. The patient in this series, aged 20 months, is, I believe, the youngest in whom the disease has been reported. Also the family here reported represent a very mild degree of involvement.

The disease has very different microscopic changes from those found in osteomalacia, osteogenesis imperfecta, rickets and Paget's disease, although these conditions are mentioned sometimes in their relation to chondrodysplasia.

Its relation to that anomaly of skeletal growth known as chondrodystrophy, however, deserves more than passing notice. In spite of the great physical deformities present in both conditions, the mental development, as a rule, is not retarded.

In his monograph on chondrodystrophia fetalis, Kaufman⁶ described three distinct varieties—the hypoplastic, hyperplastic and the malacic. He considered it a dystrophy of the cartilage concerned in the first skeletal formation during the period from the third to the sixth month of fetal life. Some of these patients died in utero, some died in infancy, others in childhood, and some lived to old age, the degree of involvement probably was the factor in determining the fate. In those that lived many variations from the typical achondroplastic dwarf were described. Opie and Allison⁷ described the case of a boy, aged 17, who had outgrowths of cartilage, microscopically similar to those found in chondrodystrophy but with no retardation of the growth of long bones. Kaufman also described two fetuses with involvement of the intracartilaginous bones of the head, but with no interference of the growth of long bones. Chondrodystrophy, therefore, may be present without dwarfing, and with widely varying degrees of involvement.

Schorr⁸ described a type of chondrodystrophy which makes its appearance at puberty, and to which he gave the name chondrodystrophia adolescentium.

From these descriptions it may be seen that chondrodystrophia exists in a variety of forms, involving those bones involved in chondrodysplasia, and with microscopic changes which are very similar and

6. Osler's Modern Medicine.

7. Opie, E. L., and Allison, N.: Hypertrophic Chondrodystrophy in Infancy and Adolescence; Progressive Anomaly of Osteogenesis, *J. Med. Res.* **36**:277, (May) 1917.

8. Quoted by Opie and Allison.

seem to differ only in degree, and there is enough similarity in these conditions to warrant the belief that there is a close relationship between them.

1. Both conditions affect bones of intracartilaginous origin without disturbing those of intramembranous origin.

2. In both conditions isolated inclusions of aberrant cartilage within and beneath the periosteum are found. Where more complete microscopic studies can be made on chondrodystrophic subjects, coming to necropsy, these irregular cartilage masses are found widely distributed in fat and in heads of bones.

3. In both conditions there is a progressive proliferation of epiphyseal cartilage, with bone formation at the edge of the proliferations, as is evidenced by the finding of irregular deposits of bone in the cartilage, in the microscopic study of growths removed.

In chondrodystrophy this proliferation of cartilage tends to widen the bone interfering with longitudinal growth, but the proliferation is in an orderly manner giving uniform enlargement, rather than the production of exostoses. The cartilage proliferation is much more excessive in chondrodystrophy, which may account for the gradual and uniform enlargement, as contrasted with the spontaneous isolated outgrowth with the resulting cartilaginous exostoses of chondrodysplasia.

4. The microscopic changes at the epiphyseal line in the two conditions present a striking similarity. In chondrodystrophy the excess of cartilage cells at the sites of ossification occur in irregular groups instead of the normal orderly arrangement in long rows perpendicular to the line of ossification. The line of ossification is straight and very narrow, and instead of a distinct zone of proliferating cartilage cells being present, they are few and unevenly distributed.

Ehrenfried was able to study a specimen from across the epiphyseal line taken from a patient with chondrodysplasia, and he described an excessive growth of intermediary cartilage, with an irregular zone of calcification, and the cartilage proliferating cells scattered in irregular groups instead of forming a distinct zone in orderly arrangement.⁹

SUMMARY

1. Many variations of hereditary deforming chondrodysplasia may occur, from the existence of multiple small cartilaginous exostoses, giv-

9. For an extensive bibliography and a review of the cases reported in American literature, the reader is referred to the article by Ehrenfried

ing the patient no trouble, to the existence of great deformities, with dwarfing, paralysis, aneurysm and malignancy.

2. The disease manifests itself in infancy.

3. The condition has much in common with chondrodystrophy of infancy and adolescence, and it is probable that a close relationship exists between them.

CALCIUM METABOLISM OF INFANTS AND YOUNG CHILDREN AND THE RELATION OF CALCIUM TO FAT EXCRETION IN THE STOOLS

PART 2.—CHILDREN TAKING A MIXED DIET *

L. EMMETT HOLT, M.D.
ANGELIA M. COURTNEY AND HELEN L. FALES
NEW YORK

In a preceding paper on calcium metabolism was considered the absorption of calcium by infants taking modifications of cow's milk and the excretion of calcium in relation to the excretion of fat in their stools. In this paper we discuss the calcium metabolism of older children taking a mixed diet. As stated in the previous paper, by calcium *excretion* is meant the total amount of calcium lost in the stools; whether part of this has been absorbed and is subsequently excreted into the large intestine is not here considered. By calcium *absorption* is meant the difference between intake and the amount lost in the stools.

HEALTHY CHILDREN

The first group considered includes children who were normal as to digestion. Tables 1 and 2 show the calcium absorption in relation to calcium and fat intake for normal children taking a mixed diet; Table 1 including the cases in which the intake of calcium oxid was high, and Table 2 those in which it was low. The values are expressed as grams per kilogram of body weight.

Calcium Absorption and Its Relation to Calcium Intake.—Excluding two unusually high values and one unusually low value, the intake of calcium oxid per kilo ranged from 0.043 to 0.178 gm., with an average of 0.108 gm. In only about one half the cases was the intake more than 0.1 gm. per kilo. The children taking a mixed diet had, on the whole, a much lower intake of calcium oxid per kilo than those who were taking modifications of cow's milk.

The absorption of calcium oxid per kilo also was much lower than was found with the infants; it ranged from 0 to 0.147 gm. of calcium oxid per kilo, the two highest values being found when the intake was exceptionally high.

* From the Laboratories of the Rockefeller Institute for Medical Research and the Babies' Hospital, New York.

* In the article published in the February issue of the *AMERICAN JOURNAL OF DISEASES OF CHILDREN*, p. 112, an error was made in the fourth line of the first paragraph of the Summary. The figure 0.6 gm. should read 0.06 gm.

TABLE I.—ABSORPTION OF CALCIUM BY HEALTHY CHILDREN TAKING A MIXED DIET, WITH AN INTAKE OF CALCIUM OXID EXCEEDING 0.09 GM. PER KILO

No.	Case	Age Yr. Mo.	Weight in Gm.	Stools	Intake of CaO Gm. per Kg.	CaO Absorbed Kg.	Per- centage of CaO Intake Ab- sorbed	Intake of Fat Gm. per Kg.	Grams CaO Intake per Gm. Fat Intake	Remarks
321	F. S.	1 6	8,975	Constipated	0.244	0.147	60.4	6.8	0.036	Very high calories per kilogram
305	H. F. 1	1 0	7,136	Constipated	0.237	0.115	48.4	4.9	0.048	
307	H. F. 3	1 0	7,749	Constipated	0.178	0.018	10.1	4.7	0.038	
318	D. L.	1 2	8,264	Constipated	0.176	0.087	49.6	4.1	0.043	High calories per kilogram, high proportion carbohydrate
267	O. W. 1	2 6	9,988	Normal	0.175	0.081	46.3	3.8	0.046	
268	O. W. 2	2 7	10,280	Constipated	0.171	0.107	63.1	3.7	0.046	
364	O. W. 4	2 7	10,546	Normal	0.170	0.104	61.4	4.5	0.038	Skimmed milk with corn oil
379	H. F. 4	1 1	8,218	Normal	0.167	0.025	15.2	4.5	0.037	Nut butter
269	O. W. 5	2 8	10,714	Constipated	0.165	0.103	62.5	5.0	0.033	Cod liver oil
368	H. F. 5	1 1	8,455	Constipated	0.163	0.033	20.3	4.2	0.039	Fat-free milk, milk butter
380	H. F. 6	1 2	8,790	Normal	0.157	0.031	32.6	4.0	0.039	Fat-free milk, nut butter
225	C. A. 1	2 3	11,800	Normal	0.156	0.033	14.6	2.9	0.053	Whole milk only. Low total calories
312	R. K. 3	3 0	11,510	Normal	0.153	0.081	52.8	3.3	0.046	
233	J. E.	3 7	10,725	Normal	0.149	0.036	21.4	2.9	0.052	Whole milk and cereal. Low total calories
232	F. W. 8	1 11	10,438	Normal	0.145	0.070	34.4	2.7	0.054	Mostly whole milk. Low total calories
327	R. M.	4 0	12,650	Acid	0.144	0.057	39.4	4.0	0.036	Tuberculous peritonitis. Had cod liver oil
296	F. M. 1	2 3	13,060	Constipated	0.142	0.036	25.5	3.0	0.047	
311	R. K. 2	1 11	11,220	Constipated	0.141	0.036	25.3	2.9	0.052	
313	E. K.	2 0	12,540	Normal	0.140	0.090	64.3	3.0	0.046	
369	W. R. 6	4 9	15,950	Normal	0.137	0.091	66.6	4.0	0.035	Corn oil, considerable milk curd in diet
295	M. M.	5 6	14,777	Normal	0.131	0.016	12.4	2.6	0.050	
309	H. F. 7	1 2	9,170	Constipated	0.128	0.019	38.5	4.3	0.029	
289	M. C.	6 0	14,300	Normal	0.128	0.048	37.1	3.1	0.041	
381	H. F. 3	1 3	9,425	Acid	0.124	0.075	60.7	4.6	0.026	
270	A. W. 1	4 0	14,358	Constipated	0.123	0.061	50.0	2.7	0.046	
317	K. P.	2 8	10,850	Normal	0.119	0.042	34.8	3.2	0.037	Diabetes insipidus. Large proportion carbohydrate in diet
328	D. D.	1 8	11,300	Acid	0.119	0.041	34.3	3.7	0.032	
277	R. L. 3	3 1	13,070	Acid	0.119	0.060	51.0	4.0	0.030	
300	P. B. 1	3 8	15,334	Normal	0.118	0.059	50.2	3.2	0.053	
320	J. O. 2	3 0	15,050	Constipated	0.117	0.064	54.6	2.6	0.046	
291	R. K.	2 1	13,150	Normal	0.114	0.051	44.7	3.2	0.035	
324	T. R.	4 0	15,395	Constipated	0.114	0.047	40.9	2.5	0.046	
366	W. R. 3	4 7	15,700	Normal	0.112	0.037	32.9	2.5	0.023	Corn oil, considerable milk curd in diet
367	W. R. 4	4 7	15,735	Normal	0.112	0.043	38.6	4.9	0.023	Corn oil, considerable milk curd in diet
264	F. W. 9	3 7	11,105	Normal	0.109	0.025	23.1	3.9	0.028	
372	F. W. 6	3 7	11,114	Normal	0.109	0.044	40.5	5.3	0.020	Fat-free milk, corn oil
330	H. F. 7	4 6	16,130	Normal	0.109	0.024	22.2	2.4	0.046	
373	F. W. 7	2 7	11,365	Normal	0.106	0.036	33.9	5.2	0.020	Fat-free milk, corn oil
276	R. L. 2	3 0	12,879	Normal	0.105	0.012	11.0	3.7	0.023	
287	W. W.	2 5	15,860	Normal	0.105	0.031	29.9	3.2	0.033	
359	R. L. 4	3 1	13,478	Acid	0.103	0.054	52.5	4.7	0.022	Corn oil Skimmed milk, cod liver oil, rather high proportion carbohydrate
326	E. A. 2	7 5	13,025	Constipated	0.096	0.041	42.4	2.6	0.037	
290	D. R.	3 0	14,150	Constipated	0.096	0.025	25.7	3.2	0.030	
322	M. J. 1	3 0	15,400	Constipated	0.093	0.058	62.2	3.1	0.030	
271	A. W. 2	4 1	14,755	Normal	0.092	0.046	50.0	3.3	0.028	

TABLE 2.—ABSORPTION OF CALCIUM BY HEALTHY CHILDREN TAKING A MIXED DIET, WITH AN INTAKE OF 0.09 GM. OF CALCIUM OXID PER KILO OR LESS

No.	Case	Age	Weight in Gm.	Stools	Intake of CaO Gm. per Kg.	CaO Absorbed Kg. per Kg.	Per- centage of Intake Absorbed	Intake of Fat Gm. per Kg.	Grams CaO Intake per Gm. Fat Intake	Remarks
		Yr. Mo.								
297	F. M. 2	2 1	13,100	Normal	0.090	0.026	28.8	2.5	0.036	
301	F. B. 2	3 9	15,705	Acid	0.090	0.010	11.3	2.7	0.033	
272	A. W. 3	4 1	15,334	Normal	0.089	0.050	56.5	3.4	0.020	Corn oil
302	F. B. 3	3 9	15,831	Normal	0.089	0.027	29.8	2.7	0.032	
298	F. M. 3	2 6	13,740	Normal	0.088	0.028	31.4	2.5	0.030	
234	A. L. 3	3 0	12,440	Normal	0.087	0.015	0.0	1.8	0.030	Fever. Low calories per kilogram
290	F. M. 4	2 6	13,979	Normal	0.087	0.018	20.5	2.9	0.030	Skimmed milk, milk butter
383	E. M. 7	2 8	11,040	Normal	0.087	0.004	4.9	2.6	0.032	Fat-free milk, nut butter
274	A. W. 5	4 2	15,725	Normal	0.087	0.012	14.0	3.3	0.026	Skimmed milk, nut butter
382	F. M. 5	2 6	11,175	Normal	0.086	0.020	23.8	2.8	0.031	Fat-free milk, milk butter
234	F. M. 6	2 7	11,130	Normal	0.086	0.001	0.8	2.7	0.032	No milk except little L. A. milk. High proportion carbo- hydrate
248	E. D.	2 6	10,305	Acid	0.084	0.018	22.1	0.9	0.089	Skimmed milk, nut butter
351	R. L. 8	4 3	11,133	Normal	0.084	0.069	11.0	3.2	0.026	
349	H. J. 1	1 4	10,889	Acid	0.084	0.042	50.6	3.3	0.026	
240	R. L. 6	4 2	11,093	Normal	0.083	0.011	12.8	3.1	0.027	Skimmed milk, milk butter
354	R. L. 7	4 3	11,215	Normal	0.082	0.092	2.6	3.0	0.027	Skimmed milk, milk butter
351	F. B. 5	3 9	14,645	Normal	0.082	0.012	8.5	3.0	0.027	Fat-free milk, milk butter
355	R. L. 9	4 3	11,698	Normal	0.080	0.029	36.4	3.0	0.027	Skimmed milk, nut butter
384	F. B. 6	3 10	14,730	Normal	0.080	0.007	0.0	2.8	0.029	Skimmed milk, nut butter
362	R. L. 10	4 3	14,815	Normal	0.080	0.005	6.8	3.0	0.027	Fat-free milk, nut butter
385	F. B. 8	3 10	15,243	Normal	0.079	0.021	26.7	2.7	0.029	Fat-free milk, nut butter
365	W. R. 2	4 7	15,442	Acid	0.077	0.025	32.2	4.2	0.018	Corn oil
352	F. B. 7	3 9	15,050	Normal	0.076	0.001	0.0	2.7	0.028	Fat-free milk, milk butter
353	R. L. 5	4 2	11,115	Normal	0.071	0.031	44.0	2.6	0.025	
350	H. J. 2	1 4	10,880	Normal	0.065	0.012	18.3	2.7	0.024	
325	C. M.	5 0	18,450	Normal	0.064	0.022	33.6	2.0	0.032	Skimmed milk. High proportion carbohydrate in diet
330	F. A. 1	7 0	11,750	Acid	0.061	0.011	18.1	2.7	0.022	High proportion carbohydrate
218	M. J. 3	3 4	15,400	Normal	0.055	0.023	42.3	2.1	0.027	High proportion carbohydrate
347	M. J. 2	3 0	15,400	Acid	0.050	0.014	27.3	2.1	0.024	
337	D. K.	4 4	18,500	Acid	0.048	0.008	38.2	2.5	0.019	
214	F. H.	3 4	11,700	Normal	0.045	0.008	16.7	1.7	0.027	Very low calories per kilogram
346	R. K.	6 0	20,500	Acid	0.044	0.017	39.3	2.3	0.020	Very low calories per kilogram
210	L. S.	3 2	16,644	Acid	0.043	0.013	30.4	1.9	0.023	No milk, high proportion carbohydrate, much vegetable and fruit
358	R. N.	5 10	20,290	Acid	0.018	0.001	0.0	1.2	0.015	

The relation of the absorption to the intake is summarized in Table 3. When the intake of calcium oxid exceeded 0.09 gm. per kilo, the absorption in most cases exceeded 0.03 gm. per kilo; the average was 0.055 gm. per kilo. When the intake was 0.09 gm. per kilo or less, the absorption in most cases was less than 0.03 gm.; the average was only 0.015 gm. per kilo. This absorption would hardly supply as much calcium oxid as is normally excreted in the urine by young children. It may, therefore, be inferred that an intake of less than 0.09 gm. of calcium oxid per kilo is insufficient to supply the calcium need of young children taking a mixed diet.

Relation of Calcium Absorption to Fat Intake.—With the older children who were taking a mixed diet, there was great variation in the intake of fat per kilo. On the whole, there was no close relation between the fat intake and the calcium absorption. When the fat

TABLE 3.—RELATION OF CALCIUM ABSORPTION TO CALCIUM INTAKE

Calcium Oxid Intake, Gm. per Kg.	Number of Observations	Absorption 0.09 Gm. or More	Absorption 0.06 to 0.09 Gm.	Absorption 0.03 to 0.06 Gm.	Absorption Less Than 0.03 Gm.
More than 0.09 gm.....	45	7	7	24	7
Less than 0.09 gm.....	34	0	0	3	31
Total.....	79	7	7	27	38

intake was high, frequently the calcium intake also was high, and consequently there was good absorption of calcium. The intake generally included less calcium in proportion to the fat than in the case of infants who were taking modifications of cow's milk. In but few instances was there more than 0.05 gm. of calcium oxid per gm. fat in the intake, and in many there was less than 0.03 gm. The highest absorption occurred when the fat intake was greater than 3.0 gm. per kilo and when for every gram of fat in the diet there was from 0.03 to 0.05 gm. of calcium oxid, that is, when the calcium intake exceeded 0.09 gm. of calcium oxid per kilo.

Percentage Absorption of Calcium.—The percentage of the calcium intake absorbed had a very wide range, varying from 0 to 66.6 per cent. When the calcium intake exceeded 0.09 gm. of calcium oxid per kilo, the percentage absorption averaged 40.4; when the intake was 0.09 gm. or less, the average absorption was only 20.3 per cent. of the intake. The excretion of calcium oxid in the stools of healthy children taking a mixed diet did not fall below a certain minimum, whatever the calcium intake. Thus the low intake of calcium oxid did not supply much excess over the amount which was normally excreted in the stools. Hence, the amount available for absorption when the intake was low was much less than the amount which was actually found to

be absorbed when the intake was ample. This explains why, with a small intake, the percentage absorption was lower than with a larger intake, since the excretion tends to remain constant at the expense of the absorption. This observation is paralleled by a similar one in regard to fat, noted in a previous paper,¹ namely, that the percentage absorption of fat was lower when the intake was small than when it was ample.

TABLE 4.—AVERAGE ABSORPTION OF CALCIUM OXID ACCORDING TO WEIGHT

Weight in Kilograms	Number of Observations	Calcium Oxid Intake, Gm. per Kg.	Calcium Oxid Absorbed, Gm. per Kg.	Percentage of Calcium Oxid Intake Absorbed
A. When Intake Exceeded 0.09 Gm. per Kg.				
7-9.....	7	0.189	0.068	36.0
9-11.....	9	0.150	0.072	48.0
11-13.....	10	0.128	0.046	36.0
13-15.....	10	0.115	0.044	38.2
15-17.....	9	0.113	0.051	45.2
Under 11.....	16	0.167	0.070	41.9
Over 11.....	29	0.119	0.046	38.7
B. When Intake Was 0.09 Gm. per Kg. or Less				
Under 13.....	5	0.076	0.014	18.5
13-15.....	15	0.081	0.013	16.1
15-17.....	10	0.073	0.020	27.4
Over 17.....	4	0.044	0.014	31.8

TABLE 5.—AVERAGE ABSORPTION OF CALCIUM OXID ACCORDING TO TYPE OF STOOL

Type of Stool	Number of Observations	Calcium Oxid Intake, Gm. per Kg.	Calcium Oxid Absorbed, Gm. per Kg.	Percentage of Calcium Oxid Intake Absorbed
A. When Intake Exceeded 0.09 Gm. per Kg.				
Constipated.....	16	0.149	0.064	43.0
Normal.....	24	0.130	0.048	36.9
Acid.....	5	0.122	0.057	46.7
B. When Intake Was 0.09 Gm. per Kg. or Less				
Normal.....	24	0.080	0.015	18.8
Acid.....	10	0.060	0.017	28.3

Relation of Calcium Absorption to Body Weight.—The absorption of calcium oxid per kilo was to a certain extent related to the total body weight, as is shown in Table 4. With an adequate intake, that is, exceeding 0.09 gm. of calcium oxid per kilo, the children weighing less than 11 kilos absorbed, on the average, about 0.07 gm. per kilo, while those weighing more than 11 kilos absorbed, on the average, only about 0.05 gm. per kilo. The infants, considered in the preceding paper, most of whom weighed less than 7 kilos, had an average absorption of about 0.09 gm. of calcium oxid per kilo. With the children taking a mixed diet whose intake was less than 0.09 gm. per kilo the absorption showed little variation with the weight.

1. Am. J. Dis. Child. 17:423 (June) 1919.

There was no constant relation between the calcium absorption and the age, irrespective of the weight.

Relation of Calcium Absorption to Type of Stool.—The relation of the calcium absorption to the type of stool is shown in Table 5. The best average absorption was found when the stools were constipated, but the average intake for this group was the highest. Acid stools were rarely found when the intake was over 0.09 gm. per kilo. In

TABLE 6.—EXCRETION OF CALCIUM BY HEALTHY CHILDREN TAKING A MIXED DIET; (1) WITH CALCIUM IN STOOLS EXCEEDING 0.9 GM.

No.	Case	Stools	CaO Intake, Gm. Daily	Fat Intake, Gm. Daily	CaO in Stools, Gm. Daily	Fat in Stools, Gm. Daily	Fat as Soap, Gm. Daily	CaO Possibly Held as Soap, Percentage of	
								CaO in Stools	CaO Intake
295	M. M.	Normal	1.94	38.8	1.70	1.56	0.53	3.1	2.7
225	C. A. 1	Normal	1.85	35.0	1.58	4.10	2.83	17.9	15.3
296	E. M. 1	Constipated	1.84	38.8	1.37	2.29	0.66	4.8	3.6
330	H. F.	Normal	1.76	38.3	1.37	1.62	0.67	4.9	3.8
234	A. L.	Normal	1.08	21.8	1.27	1.51	0.56	4.4	5.2
384	F. B. 6	Normal	1.17	40.9	1.27	2.09	1.07	8.4	9.2
301	F. B. 2	Acid	1.42	43.4	1.26	3.53	1.06	8.4	7.5
307	H. F. 3	Constipated	1.38	36.5	1.24	2.55	1.31	10.6	9.5
313	E. K.	Normal	1.75	37.8	1.24	3.57	1.51	12.2	8.6
233	F. W. 8	Normal	1.60	31.0	1.21	4.10	2.41	19.9	15.1
276	R. L. 2	Normal	1.36	48.1	1.21	1.82	1.00	8.3	7.3
254	E. M. 6	Normal	1.21	37.7	1.20	2.94	1.55	12.9	12.8
311	R. K. 2	Constipated	1.60	31.0	1.18	4.10	1.68	5.8	4.3
352	F. B. 7	Normal	1.16	41.1	1.18	2.85	1.42	12.0	12.2
366	W. R. 3	Normal	1.76	77.0	1.18	4.66	2.26	19.2	12.9
379	H. F. 4	Normal	1.36	37.3	1.17	2.56	1.03	8.8	7.5
271	A. W. 5	Normal	1.36	52.1	1.17	2.56	1.06	9.1	7.8
287	W. W.	Normal	1.67	50.9	1.17	2.40	0.99	8.5	5.9
383	E. M. 7	Normal	1.22	38.1	1.16	2.37	1.04	9.0	8.5
289	M. C.	Normal	1.83	44.5	1.15	1.70	0.71	6.2	3.9
354	R. L. 7	Normal	1.16	43.2	1.13	3.29	1.36	11.9	11.6
327	R. M.	Acid	1.83	50.5	1.11	4.35	1.23	11.1	6.7
308	H. F. 5	Constipated	1.38	35.2	1.10	1.66	1.20	10.9	8.7
362	R. L. 10	Normal	1.18	44.6	1.10	1.68	0.79	7.2	6.7
367	W. R. 4	Normal	1.76	77.0	1.08	3.87	1.35	12.5	7.7
361	R. L. 8	Normal	1.18	45.4	1.05	1.75	0.79	7.5	6.7
324	T. R.	Constipated	1.76	38.3	1.04	1.49	0.55	5.3	3.1
360	R. L. 6	Normal	1.17	43.2	1.02	1.86	0.58	5.7	5.0
351	F. B. 5	Normal	1.20	44.4	1.02	2.74	1.46	14.3	12.1
290	D. R.	Constipated	1.36	44.8	1.01	1.26	0.38	3.8	2.8
232	J. E.	Normal	1.51	28.0	0.99	1.92	1.10	11.1	7.3
302	F. B. 3	Normal	1.41	42.5	0.99	2.25	0.75	7.6	5.3
299	E. M. 4	Normal	1.22	40.1	0.97	2.53	0.90	9.3	7.4
267	O. W. 1	Normal	1.75	37.8	0.94	1.89	1.08	11.5	6.2
280	H. F. 6	Normal	1.38	35.3	0.93	2.24	0.74	8.0	4.9
264	F. W. 9	Normal	1.21	43.6	0.93	2.92	1.45	15.6	12.0
382	E. M. 5	Normal	1.22	39.2	0.93	1.84	0.66	7.1	5.4
300	F. B. 1	Normal	1.81	34.3	0.90	2.16	1.52	16.9	8.4

the few instances when the stools were acid, the intake being adequate, the average absorption was as good as when the stools were constipated or normal. Also, when the intake of calcium oxid was less than 0.09 gm. per kilo, the absorption was practically the same whether the stools were acid or alkaline, but much lower than when the intake was adequate. That the absorption of calcium oxid was dependent more on the amount of the calcium intake than on the type of stool is shown by comparing the values for the normal groups in Table 5. With high intake, the absorption was about three times

as great as with low intake. The influence of the amount of intake of calcium oxid on both the type of stool and the absorption of calcium oxid is further illustrated by three observations on one child, M. J. (Tables 1 and 2). When the intake of calcium oxid was 0.093 gm. per kilo, the stools were constipated and the absorption was 0.058 gm. per kilo; when the intake was 0.056 gm., the stools were normal and the absorption was only 0.023 gm.; again, when the intake was 0.050 gm., the stools were acid and the absorption was only 0.014 gm.

TABLE 7.—EXCRETION OF CALCIUM BY HEALTHY CHILDREN TAKING A MIXED DIET; (2) WITH CALCIUM IN STOOLS LESS THAN 0.9 GM.

No.	Case	Stools	CaO Intake, Gm. Daily	Fat Intake, Gm. Daily	CaO in Stools, Gm. Daily	Fat in Stools, Gm. Daily	Fat as Soap, Gm. Daily	CaO Possibly Held as Soap, Percentage of	
								CaO in Stools	CaO Intake
328	D. D.	Acid	1.34	41.3	0.88	1.63	0.80	9.1	6.0
270	A. W. 1	Constipated	1.76	38.4	0.88	1.43	0.67	7.6	3.8
385	F. B. 8	Normal	1.20	41.8	0.88	1.42	0.41	4.7	3.4
305	H. F. 1	Constipated	1.69	34.9	0.87	1.08	0.90	10.3	5.3
321	F. S.	Constipated	2.19	61.0	0.87	2.46	1.26	14.5	5.5
317	K. P.	Normal	1.29	34.5	0.84	1.23	0.40	4.8	3.1
297	E. M. 2	Normal	1.18	32.6	0.84	1.95	0.69	8.2	5.8
312	R. K. 3	Normal	1.76	38.3	0.83	0.95	0.39	4.7	2.2
291	R. K.	Normal	1.50	42.5	0.83	2.18	1.21	14.6	8.1
298	E. M. 3	Normal	1.21	34.1	0.83	2.53	0.94	11.3	7.8
373	F. W. 7	Normal	1.21	59.4	0.80	3.01	0.44	5.5	3.6
320	J. O. 2	Constipated	1.76	38.3	0.80	1.20	0.68	8.3	3.9
365	W. R. 2	Acid	1.18	64.5	0.80	2.57	0.97	12.1	8.1
325	C. M.	Normal	1.19	36.8	0.79	1.35	0.33	4.2	2.8
277	R. L. 3	Acid	1.55	52.1	0.76	1.18	0.25	3.3	1.6
355	R. L. 9	Normal	1.18	44.6	0.75	3.34	1.08	14.4	9.6
318	D. L.	Constipated	1.45	33.6	0.73	4.04	2.64	36.2	18.2
369	W. R. 6	Normal	2.18	63.1	0.73	1.50	0.44	6.0	2.0
309	H. F. 7	Constipated	1.17	39.8	0.72	2.71	0.73	10.1	6.2
372	F. W. 6	Normal	1.21	59.4	0.72	3.03	0.66	9.2	5.5
326	F. A. 2	Constipated	1.25	34.0	0.72	4.17	2.35	32.9	18.8
364	O. W. 4	Normal	1.79	47.5	0.69	2.10	0.93	13.5	5.2
271	A. W. 2	Normal	1.36	48.1	0.68	1.21	0.50	7.4	3.7
248	E. D.	Acid	0.86	9.7	0.67	4.42	1.83	27.3	21.3
269	O. W. 5	Constipated	1.76	53.5	0.66	3.20	1.69	25.6	9.6
359	R. L. 4	Acid	1.39	63.6	0.66	3.94	1.44	21.8	10.4
268	O. W. 2	Constipated	1.76	38.5	0.65	2.16	1.10	21.5	8.0
339	F. A. 1	Acid	0.72	32.2	0.59	1.51	0.49	8.3	6.8
272	A. W. 3	Normal	1.36	52.1	0.59	2.20	0.89	15.1	6.5
350	H. J. 2	Normal	0.71	29.1	0.58	1.35	0.40	6.9	5.6
353	R. L. 5	Normal	1.00	40.0	0.56	3.57	1.93	34.5	19.3
347	M. J. 2	Acid	0.77	32.4	0.56	4.44	0.41	7.3	5.3
345	E. H.	Normal	0.66	24.5	0.55	1.06	0.55	10.0	5.3
337	D. K.	Acid	0.89	46.6	0.55	1.31	0.07	1.3	0.8
322	M. J. 1	Constipated	1.43	45.2	0.54	1.04	0.31	5.7	2.2
336	R. K.	Acid	0.89	45.6	0.54	1.62	0.21	3.9	2.4
338	R. N.	Acid	0.36	23.9	0.51	1.43	0.40	7.9	11.1
348	M. J. 3	Normal	0.85	31.3	0.49	2.04	0.40	8.2	4.7
340	L. S.	Acid	0.69	30.5	0.48	1.58	0.52	10.8	7.5
381	H. F. 8	Acid	1.17	43.7	0.46	2.07	1.07	23.2	9.1
349	H. J. 1	Acid	0.91	35.5	0.45	1.10	0.35	7.8	3.9

Tables 6 and 7 show for the cases shown in Tables 1 and 2 the calcium excretion in the stools and its relation to the total calcium intake, to the fat intake and to the excretion of total fat and of fat as soap.

Calcium Excretion and Its Relation to Calcium and Fat Intake.—Excluding two exceptionally high values, the total daily excretion of calcium oxid ranged from 0.45 to 1.37 gm., averaging 0.87 gm. Nearly

two-thirds of the values were below 1.0 gm. The excretion was but little related to the intake of calcium oxid. When the intake was low, the excretion did not fall much below the average, so that it formed a much larger proportion of the intake than when the intake was high.

There was no evidence that a very large intake of fat was followed by an excessive excretion of calcium. In fact, no relation was shown between the excretion of calcium and the intake of fat.

Relation of Calcium Excretion to Excretion of Total Fat and of Fat as Soap.—There was but little relation between the calcium excretion and the total fat excretion. Table 6, which gives the instances in which the calcium excretion was greatest, shows only a few more instances of high fat excretion than does Table 5, which gives the instances in which the calcium excretion was lowest.

In order to bring out the relation between soap excretion and calcium excretion, averages were found for the different types of stools, since the average soap excretion varies according to the type of stool. These averages are given in Table 8.

TABLE 8.—AVERAGE EXCRETION OF CALCIUM ACCORDING TO TYPE OF STOOL

Stools		Number of Observations	Intake of CaO, Gm. Daily	CaO in Stools, Gm. Daily	Fat in Stools, Gm. Daily	Fat as Soap, Gm. Daily
A:	Constipated.....	16	1.60	0.90	2.36	1.15
	Normal.....	48	1.38	0.98	2.33	1.00
	Acid.....	15	1.06	0.69	2.45	0.74
B:	Constipated.....	16	1.60	0.90	2.36	1.15
	Normal—high calcium oxid intake....	24	1.63	1.05	2.35	1.10
C:	Normal—high calcium oxid in stools...	24	1.46	1.19	2.59	1.20
	Normal—low calcium oxid in stools...	24	1.31	0.77	2.07	0.80

Table 8 A shows that in the constipated stools there was a greater soap excretion and a smaller calcium oxid excretion than in the normal stools, although when the stools were constipated, the intake was much greater. Table 8 B, which compares with the group of constipated stools a group of normal stools when the average intake was similar, brings out more clearly the contrast between these two types of stools in calcium and soap excretion.

However, excluding the constipated stools, there was a general correspondence between the variations in calcium excretion and in soap excretion. The average for the acid stools showed a much lower soap excretion, with a much lower calcium excretion, than did the normal stools, but the intake for this group was also much lower than that for the normal group. As was previously noted in the discussion of calcium absorption, the calcium intake apparently influences to a considerable extent the reaction of the stools, a low calcium intake frequently resulting in acid stools.

The relation between calcium and soap excretion is independent of the calcium intake, as is brought out in Table 8 C, in which averages are given for two groups of normal stools arranged according to the calcium excretion. With similar intake the average soap excretion in these two groups of normal stools was exactly proportional to the calcium excretion.

Both with infants fed on milk modifications and with older children taking a mixed diet there was, as has been stated, less calcium excreted in proportion to the amount of soap when the stools were constipated than when the stools were normal. This indicates that there was on the average proportionally less calcium phosphate in the constipated than in the normal stools.

The calcium lost as soap was in most cases an insignificant part of the calcium intake. In only fourteen of the seventy-nine instances in Tables 6 and 7 did it exceed 10 per cent. In the majority of the cases it was less than 10 per cent. of the total calcium excretion, and in only eight instances did it exceed 20 per cent.

EFFECT OF VEGETABLE FATS ON CALCIUM METABOLISM

In our study of fat metabolism, one group of children were given corn oil in place of milk fat, and another group nut butter in place of milk fat. The effect of these vegetable fats on calcium metabolism is shown by the averages in Table 9.

TABLE 9.—AVERAGE ABSORPTION AND EXCRETION OF CALCIUM WITH MILK FAT AND WITH VEGETABLE FAT

Kind of Fat in Diet	Number of Observations	CaO Intake, Gm. per Kg.	CaO Absorbed, Gm. per Kg.	Total CaO Intake, Gm. Daily	Total CaO in Stools, Gm. Daily	Fat as Soap in Stools, Gm. Daily
Milk butter.....	9	0.100	0.016	1.21	1.02	1.36
Nut butter.....	9	0.100	0.015	1.23	1.06	0.79
Mainly milk fat.....	35	0.119	0.047	1.52	0.95	0.97
Corn oil.....	13	0.122	0.052	1.56	0.89	1.40

In the nut butter series the children received in other respects the same diet as during the periods in which the fat given was milk fat. Hence, the findings for these two groups in Table 9 are exactly comparable. There were no control observations to be compared with the observations on corn oil. Accordingly, an average has been found for the cases given in Tables 1, 2, 6 and 7, in which the fat in the diet was mainly milk fat and the intake of calcium was comparable with that of the children taking corn oil.

Table 9 shows that the calcium absorption and the excretion were practically the same whether the fat in the diet was milk fat or vegetable fat. *The only difference in the calcium metabolism was in the*

proportion of the calcium excreted in the form of soap. With the children taking nut butter, the soap excretion was markedly lower than with milk butter and, therefore, a smaller proportion of the calcium excretion could have been bound as soap. With the children taking corn oil the soap excretion was much greater than that of the group of children with similar calcium intake who were taking mainly milk fat. The children taking corn oil received an unusually high intake of fat, so that in respect to fat excretion the two groups are not comparable.

RACHITIC CHILDREN

All the children classed here as rachitic showed, at the time of coming under observation, marked rachitic symptoms, such as inability to stand or walk, distended abdomen and typical bone changes. With most of the children observations were made before treatment was begun, as well as during the period of recovery. Table 10 gives the absorption of calcium oxid per kilo and its relation to the calcium and the fat intake.

Calcium Absorption.—The intake of calcium oxid per kilo was high, in most cases higher than that of the majority of the normal children and in no case was it less than 0.09 gm., which, with normal children, appears to be an adequate intake. In the five observations made before treatment was begun, noted in Table 8 as preliminary observations, the absorption of calcium oxid was low, mostly below the normal average. The highest absorption occurred when the intake was very high. As the condition of the children improved, the calcium absorption increased to well above the normal average, as is shown by the later observations on all the children. With two of the children later observations (371,258) made after recovery was well established, showed a subsequent decrease in absorption. These observations confirm the conclusions of other investigators that *the absorption of calcium is low when active rickets is present, increased above the normal during recovery and falls as the need for calcium ceases to be greater than normal.* It must be remembered that by calcium absorption is here meant the difference between the calcium intake and the amount lost in the stools.

The treatment in our cases consisted in a change of the diet to include more calcium and fat by increasing the milk and giving cod liver oil or milk butter, thus furnishing an extra amount of "fat-soluble A." In the latest observations on F. W. and R. M., made after recovery was well established, vegetable fat replaced butter and cod liver oil.

TABLE 10.—ABSORPTION OF CALCIUM BY RACHITIC CHILDREN TAKING MIXED DIET

No.	Case	Age	Weight in Gm.	Stools	Intake of CaO Gm. per Kg.	CaO Absorbed Gm. per Kg.	Per- centage of CaO Intake Ab- sorbed	Intake of Fat Gm. per Kg.	Grams CaO Intake per Gm. Fat Intake	Remarks
		Yr. Mo.								
235	L. H. 2	1 6	8,270	Acid	0.288	0.160	55.4	5.5	0.053	Protein milk
245	L. H. 1	2 6	6,540	Normal	0.298	0.228	84.7	8.9	0.030	Cod liver oil, high calories per kilogram
246	L. H. 2	2 8	7,045	Normal	0.248	0.189	76.4	6.7	0.037	Cod liver oil, high calories per kilogram
316	L. R. 2	1 11	8,550	Normal	0.244	0.165	67.5	6.1	0.040	Cod liver oil just discontinued
292*	F. W. 2	3 2	9,207	Normal	0.238	0.059	24.8	3.7	0.065	
315	L. R. 1	1 10	8,205	Normal	0.223	0.127	56.8	4.9	0.046	Cod liver oil just discontinued
257	R. M. 3	2 8	9,916	Normal	0.216	0.113	52.1	6.2	0.035	Butter in place of cod liver oil of previous period. Low carbohydrate
276	R. M. 2	2 7	8,570	Constipated	0.199	0.070	45.2	6.5	0.031	Cod liver oil. Low carbohydrate
291*	F. W. 1	3 1	8,990	Constipated	0.182	0.021	11.8	2.7	0.097	
293	F. W. 3	3 4	10,110	Normal	0.179	0.097	54.1	5.6	0.032	Cod liver oil
304*	R. A. 1	4 0	7,017	Acid	0.176	0.037	26.4	5.3	0.033	
253*	R. M. 1	2 5	8,017	Acid	0.163	0.026	16.1	2.4	0.067	Protein milk and whole milk. Very low calories per kilogram
258	R. M. 4	2 10	10,625	Constipated	0.151	0.068	44.7	4.3	0.035	Olive oil in place of butter of previous period
376	R. A. 2	4 3	9,515	Acid	0.150	0.084	56.3	5.4	0.028	Extra butter
357	R. A. 3	4 4	10,393	Acid	0.138	0.079	57.9	5.6	0.024	
323*	L. H. 1	1 5	8,000	Acid	0.126	0.051	40.6	4.2	0.030	Fat-free milk with corn oil
370	F. W. 4	3 6	10,700	Normal	0.113	0.080	71.1	5.6	0.020	Fat-free milk with corn oil
371	F. W. 5	3 6	10,750	Normal	0.113	0.094	38.8	5.5	0.029	

* Preliminary observation.

In the preliminary observations, the percentage of the calcium intake absorbed was with one exception much lower than normal, but during the period of improvement, the percentage absorbed was much higher than with normal children.

The intake of fat per kilo was very high, except in some of the preliminary observations, but, in general, the ratio of the calcium to the fat of the intake was similar to that of the normal children. This resulted from the increase of both fat and calcium in the diet as a therapeutic measure.

TABLE 11.—EXCRETION OF CALCIUM BY RACHITIC CHILDREN
TAKING A MIXED DIET

No.	Case	Stools	CaO Intake, Gm. Daily	Fat Intake, Gm. Daily	CaO in Stools, Gm. Daily	Fat in Stools, Gm. Daily	Fat as Soap, Gm. Daily	CaO Possibly Held as Soap, Percentage of	
								CaO in Stools	CaO Intake
262*	F. W. 2	Normal	2.18	33.8	1.64	2.49	1.79	10.9	8.2
235	L. H. 2	Acid	2.38	45.1	1.32	5.71	2.17	20.5	9.1
261*	F. W. 1	Constipated	1.62	24.2	1.43	2.97	1.82	12.8	11.2
304*	R. A. 1	Acid	1.39	42.1	1.10	3.61	2.00	18.2	14.4
253*	R. M. 1	Acid	1.31	19.6	1.10	4.24	1.84	16.7	14.0
257	R. M. 3	Normal	2.15	61.0	1.03	6.42	2.87	27.8	13.3
256	R. M. 2	Constipated	1.70	55.7	0.93	8.59	4.19	45.1	24.7
258	R. M. 4	Constipated	1.63	47.2	0.90	7.34	3.34	37.1	20.5
263	F. W. 3	Normal	1.81	56.7	0.83	3.44	2.05	24.7	11.3
315	L. R. 1	Normal	1.83	39.8	0.79	1.96	1.23	15.6	6.7
371	F. W. 5	Normal	1.21	59.4	0.74	5.30	3.00	40.6	24.8
316	L. R. 2	Normal	2.09	52.5	0.68	3.56	2.29	33.7	11.0
356	R. A. 2	Acid	1.42	51.5	0.62	2.17	0.97	15.7	6.8
357	R. A. 3	Acid	1.42	58.1	0.61	2.33	1.26	20.7	8.9
333*	L. H. 1	Acid	1.01	33.5	0.60	2.62	0.51	8.5	5.0
266	I. H. 2	Normal	1.74	46.9	0.41	1.58	0.64	15.6	3.7
370	F. W. 4	Normal	1.21	59.4	0.35	4.01	1.39	39.7	11.5
265	I. H. 1	Normal	1.76	58.3	0.27	1.49	0.94	34.8	5.3

* Preliminary observation.

Table 11 gives for the rachitic children the calcium excretion in the stools in relation to the calcium and fat intake and to the excretion of total fat and of fat as soap.

Excretion of Calcium.—The range in calcium excretion was about the same as in the case of the normal children. There was no constant relation between the calcium excretion and the intake of either calcium or fat. On the whole, the calcium excretion was not related to the fat excretion. As with normal children, the excretion of soap was sometimes parallel with that of calcium and sometimes not. The lowest values for soap excretion were found when the calcium excretion was lowest, but the highest calcium excretion was not accompanied by the highest soap. In most cases the stools of these rachitic children contained more soap but not more calcium than those of normal children, so that the calcium lost as soap was a distinctly higher proportion of both the calcium excretion and the calcium intake than was found with normal children.

Effect of Treatment.—There was great difference in the calcium metabolism between the period of active rickets and that of recovery. Accordingly, averages are given in Table 12 representing the preliminary and the later observations. Observations 258, 370 and 371 are not included in the average, because they represent periods after recovery was well established and in which the food included much vegetable fat.

TABLE 12.—EXCRETION OF CALCIUM BY CHILDREN WITH ACTIVE RICKETS AND THOSE RECOVERING FROM RICKETS

Condition of Children	No. of Observations	CaO Intake, Gm. Daily	Fat Intake, Gm. Daily	CaO in Stools, Gm. Daily	Fat in Stools, Gm. Daily	Fat as Soap, Gm. Daily	CaO as Soap, Percentage of		Percentage of CaO Intake Absorbed	Percentage of Fat Intake Absorbed
							CaO in Stools	CaO Intake		
With active rickets. Recovering from rickets.....	5	1.50	30.6	1.17	3.19	1.59	13.6	10.6	22.0	89.6
	10	1.83	57.6	0.75	3.73	1.86	21.8	10.2	59.0	93.6

The average calcium excretion was much higher during active rickets than the normal average and during recovery somewhat lower than the normal average. The average intake of calcium oxid was somewhat higher in the period of recovery, making the percentage retention much greater. Although during recovery the fat intake was nearly doubled, the excretion of total fat and of fat as soap was but slightly increased and the percentage absorption of fat as well as of calcium was much improved.

With four of the children, the extra fat was provided by the addition of cod liver oil to the diet. With one child, additional fat was given as butter, with as good result as when cod liver oil was used. Another child showed an improved absorption of calcium on a special "protein milk" in which calcium phosphate and fat were both much increased.

CHILDREN SUFFERING FROM CHRONIC INTESTINAL INDIGESTION

Table 13 presents the findings for the absorption of calcium per kilo and its relation to the calcium and the fat intake for children suffering from chronic intestinal indigestion.

Calcium Absorption.—The intake of calcium oxid per kilo was in general lower than that of the normal children, and, except in a few instances, the absorption was extremely low. There were only four values for absorption exceeding 0.04 gm. per kilo, and these occurred when the fat intake exceeded 4.0 gm. per kilo. Only once, with as high an intake of fat, was the absorption less than 0.04 gm. per kilo. A high intake of calcium did not regularly result in high absorption.

TABLE 13.—ABSORPTION OF CALCIUM BY CHILDREN SUFFERING FROM CHRONIC INTESTINAL INDIGESTION

No	Case	Age Yr. Mo.	Weight in Gm.	Stools	Intake of CaO Gm. per Kg.	CaO Absorbed Gm. per Kg.	Per- centage of Intake Ab- sorbed	Intake of Fat Gm. per Kg.	Grams CaO Intake per Gm. Fat Intake	Remarks
322	N. C. 1	6 0	8,655	Alkaline	0.242	-0.080	0.0	2.7	0.087	Skimmed milk
323	N. C. 2	6 4	8,705	Alkaline	0.241	0.003	1.4	4.3	0.056	Skimmed milk, cod liver oil
243	H. F. 1	2 10	9,820	Acid	0.202	0.015	7.5	1.7	0.116	Low fat protein milk. Very high proportion carbohydrate
246	S. M. 1	2 10	7,685	Acid	0.191	0.113	59.2	4.8	0.040	Diet included some L. A. milk
226	G. R. 1	5 0	12,737	Alkaline	0.158	0.082	25.6	1.0	0.158	Mostly fat-free L. A. milk. Very low calories per kilogram
224	M. H. 1	2 1	7,150	Acid	0.150	0.048	43.8	4.3	0.035	
234	H. L. 1	8 0	14,302	Acid	0.144	0.031	21.7	2.3	0.062	
237	G. R. 2	5 8	14,716	Alkaline	0.140	-0.026	0.0	2.5	0.058	Lactic acid milk, very little solid food
240	F. G. 2	5 5	13,060	Acid	0.133	0.051	37.7	5.7	0.023	Lactic acid milk, cod liver oil
242	F. G. 4	6 5	17,140	Alkaline	0.114	0.007	6.2	1.9	0.050	Lactic acid milk, cod liver oil. Very low calories per kilo-gram
341	A. E.	2 9	5,165	Alkaline	0.110	0.027	24.7	3.0	0.037	Very small child, very little food
244	H. F. 2	3 3	10,600	Acid	0.106	0.017	14.5	4.0	0.027	Protein milk. High proportion carbohydrate in diet
241	F. G. 3	3 0	17,000	Alkaline	0.102	0.014	13.0	3.5	0.020	Lactic acid milk, cod liver oil
255	D. R.	2 0	16,640	Acid	0.083	0.022	26.1	2.2	0.041	Skimmed milk, cod liver oil
238	G. R. 3	7 8	23,640	Acid	0.083	0.019	22.4	2.1	0.040	L. A. milk, cod liver oil. Very low calories per kilogram
323	G. R. 2	9 4	16,560	Alkaline	0.083	0.014	17.3	2.9	0.028	Cod liver oil. Low calories per kilogram
239	G. R. 4	8 0	22,850	Alkaline	0.081	0.031	37.8	2.4	0.034	L. A. milk, cod liver oil. Low calories per kilogram
278	W. R. 1	4 6	14,630	Acid	0.071	0.004	5.8	2.4	0.020	High proportion carbohydrate in diet
343	H. L. 2	8 0	14,130	Mixed w. urine	0.042	-0.014	0.0	2.1	0.020	Very low calories per kilogram
335	E. R. 1	8 5	12,550	Alkaline	0.041	-0.015	0.0	2.3	0.018	
342	F. G. 1	5 0	10,508	Acid	0.013	0.004	28.6	2.0	0.007	No milk. Very low calories per kilogram

although in no case was there good absorption when the intake of calcium oxid was less than 0.10 gm. per kilo. The percentage of the calcium intake absorbed was, as a rule, very low.

As has been previously observed, *the absorption of calcium by infants and young children was not good unless the calcium intake bore a suitable ratio to the fat intake.* With normal children, taking a mixed diet, apparently the food should contain from 0.03 to 0.05 gm. of calcium oxid for every gram of fat, and, at the same time, the intake of both calcium and fat should be sufficient. It is seen in Table 13 that in the instances in which the calcium intake was high and the absorption poor, the ratio of calcium to fat in the intake was abnormally high. In other words, there was not enough fat in the food for the amount of calcium. In the other instances of poor absorption of calcium, the intake of both fat and calcium was too low.

TABLE 14.—EXCRETION OF CALCIUM BY CHILDREN SUFFERING FROM CHRONIC INTESTINAL INDIGESTION

No.	Case	Stools	CaO Intake, Gm. Daily	Fat Intake, Gm. Daily	CaO in Stools, Gm. Daily	Fat in Stools, Gm. Daily	Fat as Soap, Gm. Daily	CaO Possibly Held as Soap, Percentage of	
								CaO in Stools	CaO Intake
332	N. C. 1	Alkaline	2.09	23.5	2.78	3.98	1.58	5.7	7.6
237	G. R. 2	Alkaline	2.06	35.8	2.45	11.20	7.00	32.2	38.3
331	N. C. 2	Alkaline	2.10	37.6	2.07	5.09	1.83	8.7	8.7
243	H. F. 1	Acid	1.99	17.1	1.84	12.50	3.11	16.9	15.6
242	F. G. 4	Alkaline	1.95	33.0	1.83	6.19	3.50	19.1	17.9
334	H. L. 1	Acid	2.07	33.3	1.62	11.34	3.21	19.8	15.5
238	G. R. 3	Acid	1.96	49.0	1.52	7.49	4.05	26.6	20.6
241	F. G. 3	Alkaline	1.73	58.9	1.49	9.54	5.06	33.9	29.2
239	G. R. 4	Alkaline	1.85	55.1	1.15	5.11	1.92	16.7	10.5
323	E. R. 2	Alkaline	1.33	48.4	1.10	14.64	4.72	42.9	35.4
240	F. G. 2	Acid	1.73	74.2	1.06	18.67	5.06	53.3	32.7
278	W. R. 1	Acid	1.04	35.2	0.98	4.34	1.84	18.8	17.7
343	H. L. 2	Mixed w. urine	0.59	29.9	0.79	8.95			
335	E. R. 1	Alkaline	0.51	29.2	0.70	11.20	4.72	67.2	92.4
255	D. R.	Acid	0.97	23.8	0.62	4.48	2.32	37.4	23.9
294	M. H.	Acid	1.07	30.5	0.60	4.79	2.05	34.2	19.2
249	S. M.	Acid	1.47	36.7	0.60	7.30	2.67	44.5	18.2
244	H. F. 2	Acid	1.06	39.8	0.59	3.54	2.07	23.4	18.6
341	A. F.	Alkaline	0.57	15.5	0.43	1.95	1.37	31.9	21.0
342	F. G. 1	Acid	0.14	21.0	0.10	4.68	1.25	125.0	89.3

Table 14 gives for these children the calcium excretion in the stools and its relation to the calcium and the fat intake and to the excretion of total fat and of fat as soap.

Calcium Excretion.—In general, the calcium excretion was much higher than with normal children. When the excretion of calcium oxid was low, the intake was usually very low. There was no constant relation between the intake of fat and the excretion of calcium in the stools. The excretion of fat was in most cases extremely high, only once being less than 3.5 gm. The variation in the excretion of total fat and of fat as soap was entirely unrelated to the calcium excretion.

Since the excretion of soap was large, the calcium lost as soap formed a large percentage of both the calcium excretion and the calcium intake.

As the condition of chronic intestinal indigestion is characterized by the occurrence of very large stools containing a high proportion of fat, there is a temptation to withhold fat from the diet of these children. Our findings indicate that to insure a sufficient absorption of calcium, the intake of calcium must be ample and that it must be accompanied by a suitable proportion of fat. For this reason, it appears to be better to give larger amounts of fat with calcium in due proportion to children suffering from chronic intestinal indigestion, even though the loss of fat in the stools is abnormally great. As was shown previously, in our discussion of fat metabolism, these children retained a much larger amount of fat when their intake of fat was greatly increased, although their excretion of fat was at the same time increased.²

EFFECT ON CALCIUM METABOLISM OF VARIATIONS IN CALCIUM AND FAT INTAKE

Table 15 A presents a series of observations on one child, B. W., who first came under observation suffering from osteogenesis imperfecta and malnutrition. The first observation showed with a very high calcium intake an unusually high absorption of calcium. At the time of the second observation, with about the same calcium intake, the absorption had returned to normal. The child was then given 1.6 gm. of calcium acetate daily, equivalent to 0.51 gm. calcium oxid. He received this for twelve days, including the period of observation. This salt had a bad effect on the stools, which became watery, acid and showed evidences of undigested food. The absorption of calcium oxid was unchanged; the additional calcium oxid in the intake was excreted in the stools, there being no increase in the calcium excreted in the urine. The calcium acetate was discontinued, and after the stools had become normal, there was given 2.7 gm. of tricalcium phosphate daily, equivalent to 1.46 gm. calcium oxid. He received this for eight days, including the period of observation. This salt also affected the stools unfavorably, and as in the case of calcium acetate, the excess calcium oxid was all excreted in the stools.

A few months later this child was studied again. He was then considered normal as to digestion. The first observation showed excellent absorption of calcium oxid, rather above the normal average. The fat in the food was then reduced to about one half, and the loss in fat calories was made up by increasing the carbohydrates and the protein. This made the ratio of calcium oxid to fat in the intake

2. *Am. J. Dis. Child.* **18**:107 (August) 1919.

TABLE 15.—EFFECT OF VARIATION IN CALCIUM AND FAT INTAKE

No.	Age	Weight in Gm.	Stools	Intake of CaO Gm. per Kg.	CaO sorbed Gm. per Kg.	Per- cent- age of Intake per Kg.	In- take of Fat, Gm. per Kg.	Gm. of Fat per Kg. of Intake	CaO In- take, Gm. Daily	Fat In- take, Gm. Daily	CaO in Stools, Gm. Daily	Fat in Stools, Gm. Daily	Fat as Soap, Gm. Daily	CaO Possibly Held as Soap, Percentage of CaO in Stools take	CaO in Urine, Gm. Daily	Remarks
A. Observations on B. W.																
97	1 3	5,873	Softnormal	0.231	0.117	50.8	4.7	0.048	1.36	27.6	0.67	2.54	27.6	13.3	0.021	Recovering from multiple fractures
279	1 4	6,445	Acid	0.225	0.090	40.0	6.5	0.035	1.45	41.6	0.87	4.33	29.2	17.5	0.023	Cod liver oil
403	1 5	6,649	Acid	0.319	0.095	29.7	5.7	0.056	2.12	37.7	1.49	8.06	32.2	22.6	0.017	Calcium acetate (0.51 gm. calcium oxid) given daily. Cod liver oil
404	1 5	6,560	Acid-bad	0.168	0.059	21.2	6.6	0.071	3.08	43.3	2.43	Calcium phosphate (1.46 gm. calcium oxid) given daily. Cod liver oil
280	1 9	8,970	Constipated	0.234	0.106	45.4	6.2	0.038	2.09	55.5	1.14	4.57	30.2	16.5	0.026	Cod liver oil
281	1 10	10,667	Normal	0.216	0.057	23.0	2.7	0.052	2.48	27.1	1.91	3.53	11.8	9.1	0.034	Low fat, high carbohydrate. Cod liver oil
282	1 11	9,970	Normal	0.180	0.045	7.9	2.3	0.077	1.79	23.3	1.65	2.42	11.9	11.0	0.046	Low fat, high carbohydrate. Total calories reduced. Cod liver oil
283	2 0	10,888	Constipated	0.171	0.052	30.0	3.9	0.045	1.90	42.1	1.33	3.36	14.0	9.8	0.020	Proportion of fat increased. No cod liver oil
374	2 1	11,531	Normal	0.174	0.090	0.0	4.3	0.041	2.01	19.7	2.00	6.41	10.3	10.3	Fat-free milk, corn oil
375	2 1	11,566	Normal	0.174	0.098	39.3	4.3	0.090	2.01	49.8	1.22	7.01	19.8	12.0	0.047	Fat-free milk, corn oil
377	2 2	11,735	Normal	0.214	0.139	56.8	3.8	0.064	2.87	41.5	1.24	4.65	12.7	5.5	Chalk mixture (1.0 gm. calcium oxid) daily. Fat-free milk, corn milk
378	2 3	11,777	Normal	0.243	0.166	68.3	3.8	0.094	2.87	41.5	0.91	3.30	14.8	4.7	Chalk mixture (1.0 gm. calcium oxid) daily. Fat-free milk, corn milk
B. Observations on W. R.																
367	4 7	15,735	Normal	0.111	0.043	38.6	4.9	0.023	1.76	77.0	1.08	3.87	12.5	7.7	Corn oil. Milk curd
368	4 8	15,516	Normal	0.276	0.149	54.1	3.9	0.073	4.29	60.1	1.97	4.74	13.1	6.0	Same diet, less corn oil. Chalk mixture (2.0 gm. calcium oxid) daily

abnormal. The calcium absorption was much reduced, the loss of calcium in the stools becoming much greater, although the excretion of total fat and of fat as soap was less than in the preceding period. The total food was then reduced, involving a considerable reduction in calcium intake. The absorption of calcium became very low and the excretion in the stools, although less than in the preceding period, was still abnormally high. The food was then increased to give an ample and well balanced intake of fat and calcium. The absorption of calcium rose to about the normal average for children taking a mixed diet. The excretion of calcium oxid in the stools was diminished, although still higher than the normal average. The fat in the diet was then supplied entirely in the form of corn oil, and an ample intake of both calcium and fat was provided. The first observation with this diet was made only forty-eight hours after the change. There was a negative balance of calcium and a large excretion of fat in the stools. The next observation, made a few days later, showed normal calcium absorption but no decrease in fat excretion. Later, one ounce of chalk mixture (calcium carbonate), equivalent to 1.00 gm. of calcium oxid, was given daily for six days, including the period of observation. The absorption of calcium was markedly increased, becoming much higher than the normal average; also the fat excretion was diminished. A second observation was made one week later, the chalk mixture meanwhile having been continued. The absorption of both calcium and fat was further improved. Unfortunately, urinary findings were not obtained, so that it is not known whether the extra calcium absorbed was to any extent excreted in the urine.

Table 15 A shows the effect of the administration of chalk mixture with another child, W. R. This child was given 2 ounces of chalk mixture daily, equivalent to 2.0 gm. of calcium oxid for seven days, including the period of observation. As with B. W., the calcium absorption became higher than the normal average, although in this case the excretion also was appreciably increased. More than one half of the added calcium oxid was absorbed, that is, more than was absorbed in the observation on B. W.

To summarize, the points brought out in Table 15 are as follows: High absorption of calcium oxid was found with high intake of calcium oxid; calcium absorption was not increased by administration of calcium acetate or of calcium phosphate; calcium absorption was lowered by reduction of fat intake; calcium absorption was further lowered by further reduction in fat intake and reduction in calcium intake; calcium absorption was raised by increase in fat intake to restore suitable ratio of calcium to fat; calcium absorption was only

temporarily reduced by substitution of corn oil for milk in the diet; calcium absorption was greatly increased by the administration of calcium carbonate in chalk mixture.

PROPORTION OF CALCIUM AND OF SOAP IN STOOLS OF CHILDREN
TAKING A MIXED DIET

Table 16 gives the average proportions of calcium and of soap in stools of various types from children taking a mixed diet.

TABLE 16.—AVERAGE PROPORTIONS OF CALCIUM AND OF SOAP IN STOOLS OF CHILDREN TAKING A MIXED DIET

Condition of Children	Stools	Number of Observations	CaO Intake, Gm. Daily	CaO Percentage of Total Solids	CaO Percentage of Total Salts	Fat as Soap, Percentage of Total Solids
Normal.....	Constipated	23	1.62	8.3	41.8	10.1
Normal.....	Normal	45	1.38	7.7	39.1	7.9
Normal—high calcium oxid intake.....	Normal	21	1.06	9.0	42.4	9.2
Normal—low calcium oxid intake.....	Normal	21	1.13	6.3	36.3	6.5
Normal.....	Acid	18	1.19	5.1	33.0	5.9*
Normal—high fat diet, much corn oil.....	Normal	13	1.61	6.0	38.1	9.4
Normal—high fat diet, much corn oil.....	Acid	4	1.48	4.9	31.7	6.7*
Rachitic.....	Normal and constipated	10	1.85	7.7	35.9	17.4
Rachitic.....	Acid	6	1.49	6.1	39.3	10.4*
With chronic intestinal indigestion.....	Alkaline	10	1.62	8.6	38.6	18.2
With chronic intestinal indigestion.....	Acid	9	1.48	4.6	54.8	14.0*
Normal—no milk in diet.....	Acid	1	0.36	1.5	15.4	1.2*
With chronic intestinal indigestion—no milk in diet.....	Acid	1	0.14	0.6	3.7	7.9*

* Value probably too high since stools were acid.

The calcium percentage of total solids of the stools of children taking a mixed diet was considerably lower than that of the stools similar in water content of infants taking modifications of cow's milk. This is explainable by the presence of food waste, such as cellulose, in the stools of children taking a mixed diet. The constipated stools had a somewhat higher percentage of calcium than the average of all the normal stools. This was related to the calcium intake, as was shown by dividing the normal stools into two groups. The first of these corresponded to an average intake similar to that for the group of constipated stools, and showed an average value for calcium percentage of total solids even higher than that of the constipated stools. The acid stools contained a smaller proportion of calcium oxid than did the normal. Acid stools occurred more frequently when the intake of calcium was low, but difference in intake did not entirely account for the smaller proportion of calcium. This is shown by comparing the average for the group of normal stools corresponding to a low intake with the average for the acid stools. The calcium percentage of total solids was somewhat lower in the acid stools than in the normal

stools corresponding to the same intake. When the intake included large amounts of corn oil the calcium percentage of total solids of the stools was appreciably lower than when milk fat was taken. The total solids of these stools were increased by the large excretion of fat, while the calcium was not increased in proportion.

The normal stools of rachitic children contained a lower proportion of calcium than did those of normal children. With these children also the total solids of the stools were increased by high fat excretion. The acid stools of rachitic children showed a rather high percentage of calcium than the acid stools of normal children, but the intake of calcium was higher with the rachitic children.

The stools of children suffering from chronic intestinal indigestion had a lower percentage of calcium than those of normal children when the intake was similar. The lower percentage of calcium in the stools of these children, also, was due to a much increased proportion of fat.

The stools of two children who had no milk in the food and consequently a very small calcium intake showed a calcium percentage of solids in the stools far below the usual.

With mixed diet the calcium formed a smaller percentage of the total salts than with milk modifications, and the variations corresponded, in general, with the variations in calcium percentage of total solids.

With mixed diet the average soap percentage of total solids was always low and varied with the calcium percentage of total solids. With children taking large amounts of corn oil the soap percentage of total solids was proportionally higher than the calcium percentage. With the abnormal children the soap percentage was markedly higher than with normal children having the same type of stool, while the calcium percentage showed less difference from the normal.

With mixed diet the variations in calcium percentage of total solids of the stools was not related to the water content, since the stools varied little in this respect. Normally, the two factors which mainly affected the calcium percentage of total solids were the calcium intake and the reaction of the stools.

The following summary gives answers based on our observations to the questions on calcium metabolism stated in the preceding paper.

SUMMARY

1. *Normal Absorption and Excretion of Calcium.*—With children taking a mixed diet, the absorption of calcium per kilo was lower than that of infants taking modifications of cow's milk, averaging, when the intake was adequate, 0.055 gm. of calcium oxid per kilo.

The average daily excretion of calcium oxid in the stools of children taking a mixed diet was 0.87 gm.

2. *Calcium Absorption and Excretion in Relation to Calcium and Fat Intake.*—With children taking a mixed diet, the intake of calcium oxid per kilo was lower than that of the infants, the average found for seventy-nine cases being 0.108 gm. per kilo. The absorption of calcium oxid when the intake of calcium oxid was more than 0.09 gm. per kilo in nearly every case exceeded 0.03 gm. per kilo, with an average of 0.055 gm. When the intake was only 0.09 gm. per kilo or less, the absorption rarely exceeded 0.03 gm. per kilo, and in several instances there was negative balance; the average was only 0.015 gm.

The percentage of the calcium intake absorbed when the intake exceeded 0.09 gm. per kilo averaged 40.4; when the intake was 0.09 gm. or less, the absorption averaged only 20.3 per cent.

It may, therefore, be inferred that an intake of at least 0.09 gm. of calcium oxid per kilo is necessary to insure a good absorption by children taking a mixed diet.

The best absorption of calcium oxid occurred when the intake of fat exceeded 3.0 gm. per kilo, and when, at the same time, for every gram of fat there was in the diet from 0.03 to 0.05 gm. of calcium oxid. This is a somewhat lower proportion of calcium oxid to fat than was needed to insure good absorption of calcium oxid by infants taking modifications of cow's milk.

When calcium in the form of chalk mixture (calcium carbonate) was added to the diet, there was a greatly increased absorption of calcium. When calcium was added as calcium acetate or as calcium phosphate the absorption was not increased.

The excretion of calcium was not so closely related to the intake of calcium as in the case of infants taking modifications of cow's milk, and was not at all related to the fat intake.

3. *Effect of Very Small Calcium Intake.*—A very small intake of calcium resulted in either an absorption not much greater than the amount normally excreted in the urine or in a negative balance of calcium.

4. *Relation of Age and Weight to Calcium Absorption.*—The average absorption of calcium oxid per kilo was somewhat lower with the larger children, but the age, irrespective of the weight, had no constant relation to the calcium absorption.

5. *Relation Between Excretion of Calcium and Excretion of Total Fat and of Fat as Soap.*—The excretion of calcium in the stools was not at all related to the excretion of total fat, but bore some relation to the excretion of fat as soap. However, in the constipated stools, which contained the most soap, the calcium excretion was not so great as in the normal stools when the intake of calcium oxid was the same

6. *Loss of Calcium in Soapy Stools.*—The calcium lost as soap in the stools of normal children taking a mixed diet was, in most cases, an insignificant part of the calcium intake.

7. *Calcium Percentage of Total Solids of the Stools.*—The calcium formed a smaller proportion of the total solids of the stools of children taking a mixed diet than of the stools of infants taking modifications of cow's milk. The calcium percentage of total solids was lower in acid than in normal or constipated stools. The two factors chiefly affecting the percentage of calcium in the stools of children taking a mixed diet were the amount of calcium intake and the reaction of the stools. The *soap* percentage of total solids followed on the average the variation in the *calcium* percentage of total solids.

8. *Calcium Absorption and Excretion in (a) Chronic Intestinal Indigestion; (b) Active Rickets; (c) Recovery from Rickets.*—The *absorption* of calcium by children with chronic intestinal indigestion was extremely low. In the only instances in which the absorption was near the normal both calcium and fat intake were high. The *excretion* of calcium in the stools was very high, except when the intake was unusually low. The excretion of total fat and of fat as soap was very high, but was not paralleled by the calcium excretion.

The calcium *absorption* of children with active rickets was lower than that of normal children, even though the calcium intake was ample. The calcium *excretion* in the stools was somewhat higher than the average excretion in the stools of normal children.

During recovery from rickets, the *absorption* of calcium was higher than the average for normal children. This improvement accompanied the taking of cod liver oil or additional butter with a diet containing an ample amount of calcium. The calcium *excretion* in the stools of children recovering from rickets was lower than that in the stools of normal children.

9. *Effect on Calcium Metabolism of (a) Cod Liver Oil; (b) Vegetable Fats.*—Cod liver oil increased the absorption of calcium, except in cases in which the intake of calcium or of fat was very low.

The substitution of vegetable fats for milk fat did not affect the calcium metabolism of children taking a mixed diet.

A NOTE ON RENAL FUNCTION IN SCARLET FEVER *

BORDEN S. VEEDER

ST. LOUIS

AND

MEREDITH R. JOHNSTON

Captain, M. C., U. S. Army

In almost all the studies of renal function in nephritis patients have been utilized in whom the nephritis was an established condition. A few experimental studies have attempted to correlate functional changes with the type of lesion produced by the injection into lower animals of nephrotoxic substances such as uranium or bacillary toxins, and to study in a comparative way the value of various functional tests. While making some functional tests in nephritis in the spring of 1915, it occurred to us that scarlet fever was a condition which offered an exceptional opportunity to study the functional renal changes in nephritis in the human being, from before the onset throughout the various clinical phases of the condition, with particular attention to the time relationship. There is no other disease in which nephritis is such a consistent and looked for complication.

Two types of nephritis must be distinguished in scarlet fever. Early in the course of the disease, in what may be termed the first stage, an acute nephritis, of an interstitial type pathologically, not infrequently develops as a part of the clinical picture of septic infection. This is distinct from the "febrile" albuminuria met with in a very large percentage of cases at the onset of the disease. It is a definite nephritis with casts and albumin in the urine, which, in its presence or absence and in its intensity, bears a direct relationship to the degree of sepsis. As a rule, it is mild in nature and disappears when the streptococcic infection is overcome, but when there is also a necrotic angina, or severe adenitis, or otitis, etc., the nephritis may be an important factor and the kidney shows marked lesions in fatal cases. In the second stage of scarlet fever, near the end of the third week of the disease, the well known "scarlatinal" or "postscarlatinal" nephritis develops. The kidney shows extensive glomerular changes and the urine is scanty and contains quantities of albumin, casts and blood cells. Edema is common and uremia occasionally develops. There is no apparent relationship between the two types of nephritis. The first is best explained as a part of the streptococcic infection and the second

* From the Department of Pediatrics, Washington University School of Medicine.

as the result of the toxins of the scarlet fever virus itself. In studying renal function in the nephritis of scarlet fever, the two types must be distinguished carefully, as renal function varies according to the type and degree of pathologic lesion present.

REPORT OF CASES

The two cases used in this study illustrate the two types.

CASE 1 (No. 9918).—A boy, aged 2 years, was admitted to the scarlet fever ward of the St. Louis Children's Hospital, March 11, 1916. From the very onset until death, March 18, the scarlet fever ran a severe septic course with the temperature never less than 102 F., and at times as high as 106 F. The throat was deeply ulcerated, and the tonsils and the mucous membranes of the nose and throat were covered with exudate from which cultures of streptococci were obtained. On the fifth day otitis developed in both ears. The lymph nodes became tremendously enlarged and suppuration took place. Prostration was marked and the patient was usually delirious, but no meningeal complication ensued. Abscesses developed at different points about the tenth day, and a terminal broncho-pneumonia complicated the picture. It was the typical picture of a severe septic infection. Early in the course of the illness the urine showed large quantities of albumin which persisted until the end, and coincidentally pus cells and abundant casts appeared.

CASE 2 (No. 9600).—This patient, a boy, 4 years of age, had been at the country department for several months for general malnutrition. About April 11, 1916, he developed a mild scarlet fever with slight angina and adenitis. He was not at all prostrated and had a low fever for a few days. Until April 22 the urine was negative. On that day a trace of albumin was noted, and three days later a few casts were found. April 29 some edema appeared; the urine became scanty and a marked increase in the quantity of albumin was noted. Many casts and red blood cells were found microscopically. All the signs of the acute nephritis increased markedly during the next four days. A gradual improvement followed, slow at first but then with increasing rapidity, until by the end of one month only a trace of albumin and a few casts were left and no clinical sign of nephritis were present. Subsequently the urine cleared entirely.

PLAN OF STUDY

The plan of the study was as follows: Functional tests were to be made on admission. In septic cases with urinary changes these were to be repeated at frequent intervals. In mild cases, with a negative urine early in the course of the disease, weekly functional tests were to be made until either albumen appeared in the daily urine examination, or until any one of the functional tests showed a variation from the normal. The tests were then to be made at frequent intervals. In this way it might be expected to obtain information as to the curve of renal function in uncomplicated cases of scarlet fever, the curve of renal function in developing early and late types of nephritis, comparative data in regard to tests of retention and of excretion, and from these — most important — data as to time relations between functional changes as determined by retention or excretion tests and as shown by

urinary changes. It was simply necessary to study a sufficient number of scarlet fever patients who were suitable for the tests, and sooner or later we would be bound to encounter cases of nephritis. The work was started in the fall of 1915 and continued whenever suitable material was available. It was by no means possible to utilize every patient with scarlet fever, and a large number had to be dropped after one or two of the weekly tests were made. The complete program was carried through in eight cases before one was encountered in which nephritis developed (Case 1), and in nine additional cases before a second case (Case 2) was found. Fortunately, they were frank and marked cases of their respective types. In this way data were collected on seventeen cases of uncomplicated scarlet fever and on two cases of scarlet fever with nephritis. The work was continued as material became available until the spring of 1917, when all laboratory work was interrupted. As it is impossible to continue the work, it has seemed advisable to publish a note on the results so far obtained.

TABLE 1.—RESULTS IN SCARLET FEVER UNCOMPLICATED BY NEPHRITIS.
AVERAGE FOR SEVENTEEN CASES

Week	Total Nonprotein Nitrogen, Per Cent.	Phenol- sulphonephthalein Excretion, Per Cent.	Blood Pressure, Systolic
1	25.1	69.3	100
2	22.3	64	97
3	24.2	73	102
4	22.7	71	103
5	23.8	73	103

Tests for renal function, in addition to changes in the composition of the urine, are of two types. In one the ability of the kidney to excrete certain substances, such as dyes, is measured, and in the other the degree of retention or accumulation in the blood of substances normally excreted in the urine is ascertained. The phenolsulphonephthalein test was selected as an example of the first, and the total non-protein nitrogen was taken as a test of retention. In addition, the blood pressure was determined by the auscultatory method.

RESULTS

In Table 1 the results obtained in the seventeen cases of scarlet fever uncomplicated with nephritis have been averaged. The tests for the first week represent tests made from the second to the fifth day of the disease, the second week from the tenth to the twelfth day, and so

on. In all cases the diet was low in protein and creatinin free. The figures for the nonprotein nitrogen and the phenolsulphonaphthalein are all within normal figures and quite uniform throughout the five weeks. Averaging blood pressure figures requires an explanation, as in the younger children the systolic pressure averaged about 90 mm., and in the older 110 mm. The important fact was the level at which the blood pressure remained throughout the course of the disease. This uniformity of figures for the average was maintained in each individual uncomplicated case.

The data for the two nephritic cases are shown in Table 2.

TABLE 2.—RESULTS IN SCARLET FEVER COMPLICATED BY NEPHRITIS
Case 1, Early Interstitial Nephritis

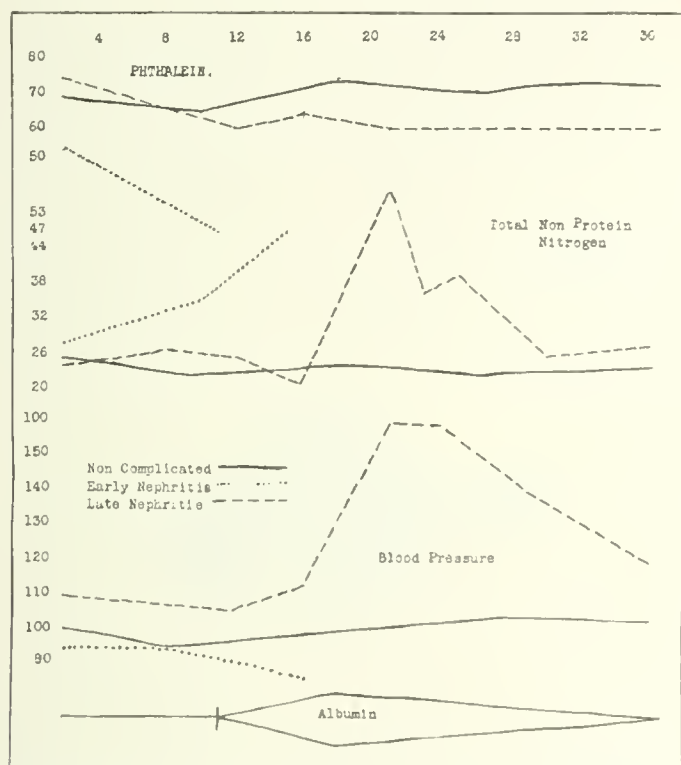
Week	Total Nonprotein Nitrogen, Per Cent.	Phenol- sulphonaphthalein Excretion, Per Cent.	Blood Pressure, Systolic
1	29	52.5	96
2	34	30	94
2½	47	Death ?	92

Case 2, Late Scarlatinal Nephritis			
Date			
4/13	21.5	75	110
4/22	Albumin in urine		
4/23	24.3	60	108
4/25	Casts in urine		
4/27	21	65	115
4/29	Edema		
4/30	39
5/ 2	53.4	60	115
5/ 4	36.8
5/ 6	39.3	60	165
5/ 9	29.8
5/11	25.5	60	138
5/23	28.4	65	110

In order to show the relative time relationship, Chart 1 has been prepared, in which the curve for the uncomplicated cases is shown by a solid line, the curve for fatal case of early interstitial nephritis is shown by the dotted line, and the curve of the glomerular scarlatinal nephritis is shown by a line of dashes.

In the early case there was rapid increase in the accumulation of nitrogenous substances in the blood from the very onset of the disease, and a corresponding decrease in the elimination of phenolsulphonaphthalein. Blood pressure was relatively unaffected.

The curve in Case 2, the glomerular type of nephritis, is more interesting. The first sign of urinary involvement was the appearance of albumin in the urine, this change being noted before any changes in the functional tests were manifest. Furthermore, the increase in the albumin and its disappearance from the urine corresponds with the development of the changes in the functional tests. Throughout the course of the disease the elimination of "phthalein" was not affected.



Time relationship in uncomplicated cases of scarlet fever and cases complicated by nephritis.

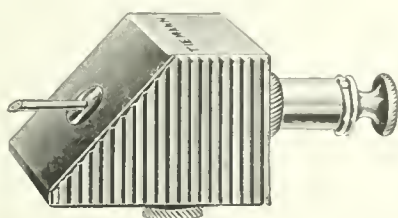
We have observed, however, in some other cases of post scarlatinal nephritis (established cases which were not followed through their development) a moderate decrease in the phthalein output at the height of the complications. Coincident with the development of the nephritis, a decided increase in the retention of the total nonprotein nitrogen took place. This retention was extremely rapid in development. The curve of increased blood pressure almost parallels the curve of nonprotein nitrogen retention.

What is most important, in our opinion, is that although the functional changes, as noted, occur in the nephritis of scarlet fever and parallel in a fairly close way the urinary changes, the albumin appeared in the urine before the changes in renal function took place. Hence, as a routine measure, the urinary examination for albumin as ordinarily carried out in scarlet fever is of more value than the functional tests in announcing the onset of an impending kidney complication.

AN IMPROVED NEEDLE FOR SINUS THERAPY*

ALTON GOLDBLOOM, M.D.
Resident Physician, Babies' Hospital
NEW YORK

About one year ago¹ I described an apparatus for puncture of the superior longitudinal sinus. This consisted of a needle 4 cm. long, with obturator, which fitted into a rectangular block 3 cm. in thickness, thereby allowing 1 cm. of needle to project. By means of a set screw, the needle was made adjustable to any desired length up to 1 cm. This apparatus has been used extensively in the Babies' Hospital for the intravenous administration of arsphenamin, physiologic sodium chlorid solution, glucose solution and sodium bicarbonate solution, as well as for the withdrawal of blood for diagnostic purposes. A slight modification has suggested itself which greatly simplifies the procedure of sinus puncture and still further minimizes the risk of injuring the wall of the sinus or the cerebral cortex.



Showing how the block of the needle is bevelled.

The original instrument entered the sinus at right angles to its long axis. A miscalculation of the depth of the sinus would make it possible to transfix the wall. For this reason the new apparatus is made to enter the sinus at an angle of 50 degrees with its long axis and pointing to the occiput. This was done by merely bevelling the block at an angle of 50 degrees, as shown in the accompanying figure. It is readily seen that an excessive length of needle in the new apparatus is not likely to damage the wall of the sinus, owing to the oblique direction in which the needle is introduced. The fact that the needle points in the direction of the blood flow is also an advantage.

The needle is adjusted to the desired length and is held in place by the set screw. The block is grasped between the thumb and index

* From the Babies' Hospital, New York.

1. Goldbloom, Alton: *Am. J. Dis. Child.* **16**:359 (Dec.) 1918.

finger of the left hand and held with the set screw pointing downward. The index finger of the right hand is used to locate the posterior angle of the fontanel. The point of the needle is then placed just over the tip of the right index finger. The finger is then withdrawn and the needle pushed in to the full depth. The obturator is then removed. When this procedure is carefully followed it is most unusual to miss the sinus. When blood does not appear upon withdrawal of the obturator it is usually due to the fact that the needle has not penetrated deeply enough. In such event, with the block still in place, the set screw is loosened and the needle gently pushed in until blood appears. With the modified instrument from 4 to 6 millimeters of needle may be allowed for young infants, and from 5 to 8 millimeters for older ones.

PROGRESS IN PEDIATRICS

REVIEW OF LITERATURE ON RESPIRATORY DISEASES

LOUIS C. SCHROEDER, M.D.

NEW YORK

INFLUENZA

Etiology.—The consensus of opinion is one expressed by Winchell and Stillman¹ in discussing the relationship of *B. influenza* to epidemic influenza. He believes that no matter what the etiologic relationship is, there can be no doubt about its importance as a secondary invader in this type of respiratory infection. The frequency of occurrence of *B. influenza* in the throats of normal persons has been as great in the period subsequent to the epidemic as it was during that time. It may persist in the throats of healthy carriers for a considerable length of time. Kolmer,² as a result of complement fixation, phagocytosis and agglutination tests, reaches the same conclusion, and shows that *B. influenza* played the most important rôle in the disease as an organism of secondary infection, if not the actual or primary etiologic agent. However, no definite proof has been submitted that *B. influenza* is the direct etiologic factor, and Lord³ says that there is no justification for that belief. Nash⁴ inquires if the liability of children and young adults is due to a streptococcus infection. If so, the epidemic resembles scarlet fever. If on the other hand, the streptococcus is the infectious agent, is it not strange that the visible changes in the throat are so little marked, for he had not seen a case in which follicular tonsillitis or enlarged cervical glands were present. Park and Williams,⁵ as soon as they discovered *B. influenza* in large number in the early cases, both in pure cultures from the lungs and in very large numbers, in and between the cells in direct smears from the tracheas examined at necropsy, concluded that whether or not this bacillus is the exciting cause, it gave evidence that it had a marked pathogenic action.

The isolation of the bacillus was no doubt attended by difficulties, and this gave rise to the many conflicting theories as to the direct

1. Winchell, Agnes J., and Stillman, Ernest G.: The Occurrence of *B. Influenzae* in the Normal Throat, *J. Exper. M.* **30**:497, 1919.

2. Kolmer, J. A., Triest, M. E., and Yagle, E.: Serum Studies on the Etiology of Influenza, *J. Infect. Dis.* **24**:583, 1919.

3. Lord, F. T., Scott, F. C., and Nye, R. N.: Relation of the Influenza Bacillus to the Recent Epidemic of Influenza, *J. A. M. A.* **72**:188 (Jan. 18) 1919.

4. Nash, W. G.: The Age Incidence of the Prevailing Epidemic, *Brit. M. J.* **2**:686 (Dec. 21) 1918.

5. Park, W. J., and Williams, A. W.: Etiology of Influenza, *Am. J. Pub. Health* **9**:45 (Jan.) 1919.

cause. Stillman¹ had the best results using an oleate hemoglobin agar with a reaction of from p_{H} 7.2 to 7.5. Bernstein and Loewe,⁶ employing gentian violet blood agar, isolated the bacillus comparatively easy, and they claim that with the use of this medium, the percentage of positive results is much higher than when plain blood agar is used.

Clinical Course.—La Fetra⁷ admits that the mortality among children was low when compared with young adults, but takes exception to the statement, made early in the epidemic, that infants and young children escaped the disease. More than nine hundred patients were seen in the last quarter of 1918, the great majority having only moderate fever after the first day, a great many having a severe tracheitis. About 10 per cent. had pneumonia, and of these about one half died. Clinically, the cases were divided into several main divisions:

1. Those with high fever and prostration but without physical signs of any localization.
2. Cases with rhinitis or pharyngitis or both.
3. Cases with tracheitis or laryngitis.
4. Cases with bronchitis.
5. Cases with pneumonia.

In the last group, four-fifths were cases of bronchopneumonia. Cyanosis was not as frequently present as in adults. Six patients had interstitial emphysema. In the matter of blood counts there were great variations, but the leukopenia of adults was not characteristic in children.

Achard⁸ describes thirty-two cases occurring in children less than 2 years of age. Thirteen of these had pneumonia. He believes that influenza in infants is by no means exceptional, that the forms of the disease may differ and the gravity vary. Infants do not possess any real immunity. Speaking only of general impressions, Locke⁹ thinks that the death rate appears to be high for those under 5 years of age, to decrease sharply to the age period of from 15 to 19 years, when it increases rapidly to the maximum, in the period of from 30 to 34 years. The series of pneumonia cases following influenza seen at the Babies Hospital in New York, according to Wollstein,¹⁰ was far more severe,

6. Bernstein, E. P., and Loewe, L.: A Simple Method for the Isolation of the Influenza Bacillus, *J. Infect. Dis.* **24**:78 (Jan.) 1919.

7. LaFetra, L. E.: Some Clinical Manifestations of Influenza in Children, *Am. J. M. Sc.* **157**:770 (June) 1919.

8. Achard, C.: Influenza in Infants, *Brit. J. Child. Dis.* **16**:78 (April-June) 1919.

9. Locke, E. A., Ronne, G. E., and Lande, H.: The Clinical Aspects of the Recent Influenza Epidemic, *Boston M. & S. J.* **180**:124 (Jan. 30) 1919.

10. Wollstein, M., and Goldbloom, A.: Influenza in Infants, *Am. J. Dis. Child.* **17**:165 (March) 1919.

more extensive and more highly fatal than any other group of pneumonia cases observed in the hospital over a similar period of time. Eighteen cases which came to necropsy form the basis of her study. In this series of cases a definite leukocytosis was found in ten, no increase occurred in five and a leukopenia was present in one syphilitic infant. The eighteen cases showed a variety of lesions making a characteristic picture of congestion, edema, general bronchitis, scattered pneumonia lesions differing in age but involving two or more lobes, subpleural hemorrhages and pleural exudate. Capillary hemorrhages in the other viscera were constant.

The influenza bacillus was grown in every case, but not alone. Pneumococcus Type IV was the bacterium most frequently associated with it. During life the sputum contained *B. influenzae* in thirteen out of seventeen cases in which it was searched for.

Montgomery¹¹ concludes that the tendency in uncomplicated cases of influenza in infants and children is toward a leukopenia rather than a leukocytosis, and that there is only a slight leukocytosis in complicating pneumonia. In his entire series there was a leukocyte count of less than 10,000 in the fatal pneumonia cases. The differential counts showed nothing that could be of help in either prognosis or diagnosis.

In considering the clinical course of influenza in children, Ostheimer¹² lays particular stress on the uniform drowsiness, even stupor, noticed in all his cases. This, with the fever, was noticed in every case, regardless of age. The next common symptom was loss of appetite, noted in 69 per cent. Some of the older children continued to eat well, in spite of the evidences of toxemia. The aches and pains so commonly described in adults were present in only 27 per cent.—among the older children—as was to be expected. Smith¹³ divided his cases into three clinical groups.

1. Temperature elevation with minor symptoms.
2. Temperature elevation with vomiting as the main symptom.
3. Temperature elevation with coryza or cough as the main symptom.

Complications and Sequels.—Many of these, other than pneumonia, have been reported. From a group of children who were suffering from influenza and who had an unusual clinical entity, namely, "influenzal croup," Regan¹⁴ selected twenty for study. From

11. Montgomery, J. C., and Dunham, E. C.: Leukocyte Counts During Influenza in Infants and Children, *Am. J. Dis. Child.* **18**:153 (Sept.) 1919.

12. Ostheimer, M.: Influenza in Children, *Med. Clin. N. Am.* **2**:743 (Nov.) 1918.

13. Smith, A. D.: Influenza and Bronchopneumonia in Children, *Arch. Pediat.* **36**:214 (April) 1919.

14. Regan, J. C., and Regan, K.: Influenzal Croup, *Am. J. Dis. Child.* **17**:377 (June) 1919.

the close resemblance of their symptoms to diphtheria many were at first admitted to the contagious ward. Later, because of the constant absence of a membrane, the failure to respond to antitoxin and the uncertain effects of intubation, made it necessary to consider some other etiologic factor than diphtheria. Symptoms previous to admission were the usual ones of influenza. From two to ten days later, the signs of croup appeared. In a few cases the first symptom was a croupy cough, which became progressively worse, associated with symptoms of laryngeal stenosis.

Clinical Course.—This depended on the extent and severity of the laryngeal involvement and the presence or absence of a complicating pneumonia. It was common for the symptoms of laryngeal stenosis to progress to a point of impending asphyxia. When pneumonia is present, the laryngeal stenosis dominates the clinical picture. Certain of the symptoms differ from the croup of diphtheria. There is no membrane, and the mucous membrane is dry and glistening, in contrast to the moist appearance in diphtheria. It is most frequent between three and ten years, is more common in boys than in girls, and the mortality is low, five deaths in a series of twenty cases. Stenosis was present in all cases, and in all but three cases pneumonia occurred.

Klebs-Loeffler bacilli were not found. The bacterial flora was very similar to that noted in influenza cases. From the nasopharynx the Pfeiffer bacillus, the pneumococcus and *Micrococcus catarrhalis* were obtained. In postmortem cultures from the larynx and trachea, the staphylococcus was most constant, the Pfeiffer bacillus and the pneumococcus being next in order of frequency. In cultures from the lung, the Pfeiffer bacillus was predominant, with streptococci and staphylococci present in lesser numbers. A varied blood picture was seen. Leukopenia occurred, but was not constant. A moderate leukocytosis was most constant, as the frequency of pneumonia would lead one to expect.

The nervous system did not escape, but D'Espine¹⁵ saw no suppurative meningeal cases during the epidemic, but describes briefly cases reported by Brat and Fobler in which influenza bacilli were grown from the spinal fluid. The cases with nervous complications seen by him were divided into two groups, one a meningeal form and the other a convulsive or eclamptic form. The former shows distinct changes in the spinal fluid, with apathy and cerebral nerve palsies. The latter show no changes in the spinal fluid, except increased pressure, but are characterized by convulsive seizures and a rapidly fatal outcome. Neal¹⁶ draws attention to three points in reviewing the cases

15. D'Espine: Nervous Complications of Influenza in Children, Arch. de méd. d. Enf. **22**:1 (Jan.) 1919.

16. Neal, J. B.: Meningeal Conditions Noted During the Epidemic of Influenza, J. A. M. A. **72**:714 (March 8) 1919.

of meningeal involvement during the influenza epidemic: (1) Very few cases of meningitis have been due to the influenza bacillus. (2) A larger percentage of cases of epidemic meningitis was seen than is usual. Cultures of the spinal fluid were made in blood as well as glucose ascitic agar to see if any hemoglobinophilic bacilli were present with the meningococci, but there was no evidence of a mixed infection. (3) Twenty cases of influenza meningeal symptoms developed, usually during convalescence. The spinal fluid is different from the meningism occurring in pneumonia, gastro-intestinal conditions, and acute infections in children. It is clear, under pressure, with a slight to a marked increase in the number of cells, with a preponderance of mononuclears, an increase in the albumin and globulin, a normal Fehling's reduction and no organisms.

Johnson¹⁷ reports a case in which the spinal fluid was cloudy and the culture of the fluid showed influenza bacilli and a predominance of polymorphonuclear cells. This occurred in a boy aged 3 years, who had influenza. Convalescent serum was used at three different times with a complete recovery. The so-called encephalitis lethargica undoubtedly belongs in the first group of D'Espine's.¹⁵ A typical case of this puzzling condition is reported by Sharfin.¹⁸ The patient, a 15-months-old infant, died.

Menninger¹⁹ and Barnes²⁰ describe the mental disturbances and psychoses noted as being postinfluenzal, but make no mention of any children being affected.

Davies²¹ reports three cases of nephritis which he thinks are of interest since they all occurred in females under 15 years of age (3, 10 and 14 years), and all cases started on the fourth day of an attack of influenza. He believes that chronic nephritis is a much more common sequel of influenza, but these cases show the importance of examining the urine during such epidemics.

Laessle²² and Payne²³ had different experiences with the nasal and pharyngeal sequels of influenza. The former took cultures in all

17. Johnson, C. K.: A Case of Influenza Meningitis, *Arch. Pediat.* **36**:82 (Feb.) 1919.

18. Sharfin, Z.: Encephalitis in an Infant Following Influenza, *New York M. J.* **109**:576 (April 5) 1919.

19. Menninger, K. A.: Psychoses Associated with Influenza, *J. A. M. A.* **72**:235 (Jan. 25) 1919.

20. Barnes, F. M.: Psychoses Complicating Influenza, *J. Missouri M. A.* **16**:115 (April) 1919.

21. Davies, A. L.: Acute Nephritis Following Influenza, *Brit. M. J.* **1**:73 (Jan. 18) 1919.

22. Laessle, H. A.: Nasal and Pharyngeal Sequels of Influenza, *Laryngoscope* **29**:103 (Feb.) 1919.

23. Payne, E. M.: Nasal Diphtheria and Epidemic of Influenza, *Brit. M. J.* **1**:7 (Jan. 4) 1919.

cases that seemed suspicious, with absolutely negative results, while the latter is convinced that the high mortality during the epidemic was owing, in no small measure, to nasal diphtheria which was unrecognized. He reports eight cases occurring among influenza patients in which positive cultures were obtained.

Levin²⁴ thinks that postinfluenzal alopecia is very common, and reports the case of a girl, aged 14 years, as being typical of many cases seen by him. The alopecia usually appears from three to eight weeks after an attack, and is characterized by a sudden thinning and falling out of the scalp hair, and occasionally by areas of incomplete baldness. The prognosis is usually good.

Of the total number of cases of influenza seen at the South Side Hospital²⁵ the eye department was called in to see 16 per cent. These were for the greater part cases of acute congestion of the ocular conjunctiva, not a catarrhal type, but marked by a dilatation of the bulbar conjunctival vessels, with some edema of the conjunctiva.

Bronson²⁶ notes the fact that catarrhal jaundice has always been associated with influenza, yet very few cases have been published in the epidemic. He has notes on twelve children who had a definite exposure to the disease and developed jaundice, but did not develop any signs of the disease itself.

TREATMENT

Prophylaxis.—Classes on the prevention of respiratory diseases²⁷ have been organized by the department of health of New York City. These classes consist of mothers of enrolled babies and the "Little Mothers," the elder sisters of the station babies. The basis of this work is the instruction given by the department nurses, relating to all the means taken to prevent respiratory infections. Special emphasis is laid on the general cleanliness and ventilation of all the stations, the evils of overcrowding, the avoidance of bringing to the clinic other children than those to be examined, distributing the visits over the entire morning, instead of congregating at one time; group inspection each morning, excluding those with the least sign of respiratory infection, both children and adults, the isolation of children and adults taken ill and the great danger of hand to mouth infection.

24. Levin, O. L.: Postinfluenza Alopecia, New York M. J. **109**:409 (March 8) 1919.

25. Stieren, E.: Ocular Lesions of Influenza, Am. J. Ophth. **2**:55 (Jan.) 1919.

26. Bronson, E.: Catarrhal Jaundice Associated with Influenza in Children, Brit. J. Child. Dis. **16**:78 (April-June) 1919.

27. Weekly Bull. Dept. Health, New York City, Oct. 11, 1919. Preparedness at Baby Health Stations Relative to Influenza.

The use of masks did not meet with much approval. Hill²⁸ thinks that the use of a mask, by raising the temperature and humidity of the air breathed, is against the natural defensive mechanism, and he urges the deep breathing of cool air brought about by exercise and sleeping in the open air; and as an adjunct, the use of any spray, gargle or snuff, which enhances the outflow of secretion from the respiratory membranes of the nose and throat. Barnett²⁹ concludes that the wearing of masks is of little value. Their use did not reduce the number of new cases.

Burton³⁰ had 300 cases of influenza without a complicating pneumonia, and no deaths. He kept them in well ventilated rooms, at an even temperature of 70 F. It is his belief that the influenza bacilli are clinically destroyed or influenced by the temperature to the extent that they will not infect the nurse or persons who may be exposed to the germs of the patient.

La Fetra⁷ found nothing specific to combat the disease directly. The vaccines, even for prophylaxis, were not definitely advantageous. The general plan was to have complete rest in bed until the temperature was normal for four or five days. The hot tub, used three or four times a day, was very efficacious. The temperature of the bath should be two or three degrees below the temperature of the patient, and the body should be rubbed thoroughly while the patient is in the tub. For the catarrhal inflammations of the upper respiratory tract, steam inhalations with the addition of creosote proved the most useful. Patients with bronchopneumonia, who have mouth breathing from dyspnea or nasal obstruction, fare much better in a warm, moist atmosphere. After spasmodic contractions are overcome the fresh air treatment is of advantage. For the lobar pneumonias, cold air is of advantage, if there is no nasal obstruction. Digitalis is usually of much help. The course of the disease is very uncertain, and relapses and reinfections of different systems are not infrequent.

Ostheimer,¹² outlining the treatment for infants, lays stress on plenty of fresh air, outdoors on sunny days and the use of magnesium sulphate, from one to four tablespoonfuls, diluted, every morning while the fever lasts. The coal tar products and Dover's powders, reported to be very useful in adults, were not found necessary.

The use of vaccines has been disappointing, although Rosenow,³¹ in describing the effects obtained, thought it was possible to obtain a definite degree of protection.

28. Hill, L.: The Defense of the Respiratory Membrane Against Influenza, *Brit. M. J.* **1**:238 (March) 1919.

29. Barnett, N.: Masking an Entire School to Prevent the Spread of Influenza, *Arch. Pediat.* **36**:83 (Feb.) 1919.

30. Burton, S. L.: Uniform Temperature in the Prevention of Influenza and Pneumonia, *Southwestern Med.* **2**:11 (Feb.) 1919.

31. Rosenow, E. C.: Prophylactic Inoculations Against Respiratory Infections, *J. A. M. A.* **72**:31 (Jan. 4) 1919.

O'Malley and Hartman³² report forty-six cases treated by plasma from convalescent patients, and they believe that the toxemia was neutralized this way.

Acidosis, according to Ely,³³ was the chief cause of death during the epidemic. He firmly believes that all patients must be treated for possible acidosis, and to this end advises the use of sodium bicarbonate, potassium citrate and lime water, both at the onset and during the attack.

Prognosis.—This was undoubtedly better in children than in adults, but that it had to be a guarded one is well illustrated by a case reported by Garret.³⁴ A four-year-old child, who had had influenza two weeks before, had only a slight cough which was improving. One morning, while dressing him, his mother noticed that his body was swollen. At 11 a. m. the trunk, neck and eyelids were swollen and doughy, but no crackling could be elicited. At 12:45 p. m. the swelling had extended to the middle of the forearms and down the thighs almost to the knees. A tympanitic note could be obtained over any part of the swelling, and emphysematous crackling could be elicited on palpation. The swelling of the eyelids was very marked, and the scrotum was blown up to the size of a billiard ball.

At necropsy, pus was found at the bifurcation of the trachea and could be squeezed from the left bronchus. On opening the bronchus, a perforation about one-sixteenth of an inch in diameter was discovered just beyond the bifurcation of the trachea, apparently connected with what seemed to be a suppurating lymph node.

Friend³⁵ thinks that the extraordinary immunity from influenza among 800 boys at Christ's Hospital school was due, in the main, to the following factors:

1. The physical training, which, although it had been undertaken for only six months, had already produced a marked improvement in physique.

2. The nasal drill, which is perhaps the most important of all. This drill was devised by Ormiston³⁶ and consists, in the main, of the class room use of the handkerchief and the application of a powder to the nasal membrane to produce free sneezing.

32. O'Malley, J. J., and Hartman, J. W.: Treatment of Influenza Pneumonia with Plasma of Convalescent Patients, *J. A. M. A.* **72**:34 (Jan. 4) 1919.

33. Ely, T. C.: The Alkali Treatment Applied to the Acidosis of Epidemic Influenza, *New York M. J.* **109**:573 (April 5) 1919.

34. Garret, R. R.: Surgical Emphysema Due to Perforation of the Left Bronchus, *Brit. M. J.* **2**:686 (Dec. 21) 1918.

35. Friend, G. E.: Apparent Immunity from Influenza at a Public School, *Lancet* **1**:105 (Jan. 18) 1919.

36. Ormiston, I.: Treatment of Adenoids, *Lancet* **2**:240 (Aug. 24) 1918.

3. The fact that for the past three months the caloric value of the school diet has reached practically the pre-war value of 3,000 calories per boy per diem, for the first time since 1916.

4. The effect of inoculation, both therapeutic and moral. The vaccine used was a polyvalent influenza bacillus vaccine. Mixed vaccines were not used because pneumonia and streptococcus infections were regarded as complications, occurring in the majority of cases after the onset of an influenzal infection.

PNEUMONIA

Cohen³⁷ and his co-workers have reported some of the results of their studies in pneumonia. They believe that a poison can be demonstrated in the pneumonic lung which is not found in the normal lung. This poison, injected into animals, produces toxic symptoms and prompt death.

Quinin hydrobromid exerted a very marked neutralizing action on the toxicity of the poison isolated. In therapeutic doses it prolonged the life of the animal up to five days after the injection of the lethal dose. Quinin hydrochlorid and quinin, and urea hydrochlorid and ethylhydrocuprein (optochin) afforded less protection. These two points, i. e., the proof of a pneumonic lung poison and its partial conquest by quinin, are new phenomena, and the demonstration is the result of cooperation between the clinician and the laboratory man.

His summary of a definite method of treatment is as follows: Pneumonia patients are benefited by quinin, as shown by clinical and experimental evidence. We can do more good if we give quinin plus digitalis, than if we give digitalis alone, and we can do still more good if we give quinin plus digitalis, plus pituitary extract, than if we leave out the latter. The treatment is not antipyretic, but the temperature is an index to the quinin effect. Pituitary extract, by keeping up the blood pressure, prevents distention, and the indication for pushing digitalis is found in the relationship of diastolic blood pressure to respiration frequency. It is wise to start the digitalis early in order to sensitize the neuromuscular apparatus of the heart.

Alkaline saline drinks or artificial mineral waters should be given freely to keep the urine neutral to litmus.

Behrend³⁸ calls attention to the necessity of keeping the distinguishing features of the chest versus the abdominal conditions in mind.

37. Cohen, S. S.: Some Recent Results of Coordination of Laboratory and Clinical Researches in Pneumonia, *Pennsylvania M. J.* **22**:506 (May) 1919.

38. Behrend, M.: Pneumonia, Acute Empyema, Acute Appendicitis, Pneumococcus Peritonitis; Their Differential Diagnosis, *Med. Rec.* **95**:102 (Jan. 18) 1919.

Mistakes are made and children are usually the sufferers. Physical signs must assist, but more stress must be laid on inspection, there being only one exception to this observation, when rapid breathing will lead one astray, namely, in that rare condition known as pneumococcus peritonitis. The leukocyte count will be high in both diseases, but it is usually higher in pneumonia. He thinks it would be wise to disregard the blood counts in the differential diagnosis of these diseases.

Lord,³⁹ as a result of his investigations to determine the influence of varying hydrogen ion concentrations on the proteolytic activity of cellular material obtained from pneumonic lungs, shows that a proteolytic enzyme is present which digests coagulated blood serum at hydrogen ion concentrations of 7.3 to 6.7 and is inactive at higher, i. e., more acid, concentrations. Evidence is also brought forward of a peptone splitting enzyme, operative at hydrogen ion concentrations between 8.0 to 4.8, but most active between 6.3 and 5.2.

The phenomenon of resolution may thus be explained. It is highly probable that during the course of the disease the hydrogen ion concentration of the exudate gradually increases. With the breaking down of the cellular material an enzyme digesting protein (fibrin), in weakly alkaline and weakly acid mediums, may be liberated. With the gradual increase of the hydrogen ion concentration of the pneumonic lung the action of this enzyme probably ceases. An enzyme, capable of splitting peptone to amino-acid nitrogen is probably active during the proteolysis of the fibrin and further activated when the hydrogen ion concentration of the pneumonic lung is increased to within range of its optimum activity, at a p_H of 6.3 and 5.2. By this means it may be conceived that the exudate is dissolved and resolution takes place.

Continuing the study of the relation of the pneumococcus to hydrogen ion concentration, Lord and Nye⁴⁰ reach the conclusion that the production of acid is the most important factor in the growth and death of pneumococcus in fluid mediums containing 1 per cent. glucose.

Stadie⁴¹ found no unusually low oxygen capacities while studying the cyanosis of influenza pneumonia, even in the fatal cases, and therefore concludes that methemoglobin formation can hardly have occurred to such an extent as to be a factor.

39. Lord, F. T.: The Relation of Proteolytic Enzymes in the Pneumonic Lung to Hydrogen Ion Concentrations. An Explanation of Resolution, *J. Exper. M.* **30**:379 (Oct. 1) 1919.

40. Lord, F. T., and Nye, R. N.: The Relation of the Pneumococcus to Hydrogen Ion Concentration; Acid Death Point and Dissolution of the Organism, *J. Exper. M.* **30**:389 (Oct. 1) 1919.

41. Stadie, W. C.: The Oxygen of the Arterial and Venous Blood of Pneumonia and Its Relation to Cyanosis, *J. Exper. M.* **30**:215 (Sept. 1) 1919.

Cecil⁴² found pneumococcus vaccine of great value. Among the indications to which he calls attention is the use of it in large institutions, such as orphanages. He believes that the incidence rate of pneumonia would undoubtedly be lowered.

EMPYEMA

Churchill⁴³ says that this complication is relatively infrequent. The onset is insidious; early diagnosis is difficult; late diagnosis, with a considerable amount of fluid present, is easy. A displaced apex beat is an important sign. He draws attention to the fact that fluid is found not infrequently in the pleural cavity before crisis, the "pleuresie parapneumonique" of the French. Thus, Jerdine found fluid in 40 per cent. of a small series of cases of pneumonia before the crisis. One to five c.c. of a sterile serofibrinous fluid was obtained on aspiration. This represents the beginning of a possible empyema. Fortunately, few cases "ripen" and the fluid presumably is absorbed. Empyema occurs in about five in one hundred cases, and while this is a very low percentage, the danger signals must be watched for carefully. These are: the child looks sick; is drowsy; begins to have a septic look; the respiratory curve stops its downward convalescent course, remains stationary and then begins to creep up, even before the pulse and temperature have been noted to have changed, the breathing not necessarily being labored.

The conditions likely to be confused with empyema are: unresolved pneumonia; pneumonic abscess and pericardial effusion. Unresolved pneumonia usually gives a dull rather than a flat note; louder and more distinct bronchial respiration; râles, crepitant, subcrepitant and fine moist, and a considerable degree of bronchophony.

Pulmonary abscess is rare in children. Persistent amphoric respiration and a tympanic quality to the percussion note over a limited area point to this lesion.

Pericardial effusion may simulate a left-sided effusion. The area of dullness, however, is peculiar, being pear-shaped; the heart sounds are muffled and indistinct. A displaced heart beat is an important sign, and in all cases in which fluid is suspected, the exploratory needle should be used repeatedly, if necessary.

Bezy and Escaude⁴⁴ present two cases with the hope that it will prevent or help eliminate some of the errors which are made in con-

42. Cecil, R. L.: The Present Status of Pneumococcus Vaccine, *Am. J. Pub. Health* **9**:589 (Aug.) 1919.

43. Churchill, F. S.: Empyema in Children with Special Reference to Diagnosis, *Boston M. & S. J.* **181**:87 (July 24) 1919.

44. Bezy, P., and Escaude, F.: Latent Purulent Pleurisy in Young Children, *Arch. de méd. d. Enf.* **22**:137 (March) 1919.

sidering purulent pleurisy in children. A three-year-old child had had at eighteen months what had been diagnosed bronchitis and pertussis. The child was never well after that, and was considered to have a tracheobronchial adenopathy. Months later a swelling appeared in the axilla which ruptured spontaneously and discharged pus at intervals. The case was then diagnosed as tuberculosis of one of the ribs, but a fuller consideration of the case, helped out by the roentgen ray, led to a diagnosis of purulent pleurisy. Resection of the rib was followed by a quick and complete recovery.

The second case was in a two-year-old boy who gave physical signs of empyema, but in whom two exploratory punctures were negative. A tumor-like swelling appeared later in the left mammary region, puncture of which proved the presence of pus, which contained pneumococci. Rib resection resulted in a cure.

Special emphasis is laid on the necessity of repeated roentgen-ray examinations of all difficult, long-standing chest cases.

The treatment of empyema has been the subject of many papers lately. The report of the United States Army Empyema Commission leans more to the wider employment of the Carrel-Dakin method than to any other single method, but as yet, reports of its use in children are very meager. Brooks⁴⁵ reviews the newer methods of treatment, including the repeated aspirations following with injections of neutral solution of chlorinated soda, a closed method used at Walter Reed Hospital and the Carrel-Dakin treatment as carried out at the Rockefeller Institute.

Lilienthal⁴⁶ thinks that in deciding on the primary operative procedure in any case of empyema, the first thing to consider is whether or not it is the mechanical pressure of the purulent fluid on the circulatory apparatus in the thorax, with the displacement of the heart, which is causing the cyanosis and respiratory embarrassment so frequently noted. The loss of respiratory area is not enough in itself to account for these symptoms, nor is the sepsis. Relief of pressure is the first crying need and must be secured as soon as possible. If the patient is acutely ill and in great distress with seropurulent exudate, the thorax can easily be emptied without shock by what is known as air replacement aspiration. This, in fact, is not at all an aspiration in the true sense of the word, but a mere evacuation of the fluid by means of a small trochar and cannula which permits the fluid to escape and a certain amount of air to replace it without the powerful vacuum force of the usual Potain or other suction apparatus.

45. Brooks, C. D.: Treatment of Empyema, *J. Mich. M. S.* **18**:107 (March) 1919.

46. Lilienthal, H.: The Selections of Operative Methods in Empyema of the Thorax, *New York State J. M.* **19**:359 (Oct.) 1919.

In commenting, in his summary, on the Carrel-Dakin method he says that the method may be employed with excellent results when the cavity is simple and the lung expansile. It is not to be used in complicated cavities when the tubes cannot be made to reach every part.

Emerson⁴⁷ claims that among certain points of great importance in the surgical care of empyema, one that is still not clearly recognized is that no operation should be performed early. So long as the quantity of pus is not so large that by its mere bulk it interferes with the action of the heart and lungs, there is no great hurry in removing it.

Chevrier⁴⁸ believes that the logical treatment of purulent pleurisy is the use of a disinfecting gas or vapor combined with a double thoracotomy. He lays much stress on the necessity of having the patient in the proper position, claiming that in the empyema operations as usually performed not enough attention is paid to the proper emptying of the costophrenic sinus nor the costovertebral groove. His proposed technic is described in detail and well illustrated.

Thomas⁴⁹ describes the essential features of an encapsulated empyema rupturing into the pleural cavity. It usually occurs during the course of a normal convalescence, being ushered in with a sharp pain in some part of the chest, brought on by slight exertion. In a few hours, the patient becomes critically ill with a rise in temperature, rapid pulse and increasing dyspnea. The abdomen is found to be greatly distended and a generalized tenderness is present. The patient becomes progressively worse with no change in the picture, except an increasing prominence of the signs of fluid in the chest.

BRONCHIITIS

Patterson⁵⁰ considers it timely, in view of the transference of the peanut from a delicacy into a more staple article of diet, to draw attention to and consider the seriousness of the peanut as a foreign body in the bronchi. Six cases are reported, all in children less than two years of age. Attention is drawn to the fact that septic pneumonia often follows in this class of foreign bodies; that small fragments of peanuts at times are held in the swollen mucosa, and that they are not coughed up. Often in cases where the foreign body is opaque to the roentgen ray the physical signs are the sole reliance; but too often the signs are considered indicative of the lesions present, but the foreign

47. Emerson, C.: Treatment of Empyema by the Closed Method, *Nebraska M. J.* **4**:65 (March) 1919.

48. Chevrier, L.: Study on the Drainage of the Pleura, *Presse méd.* **27**:9 (Jan. 9) 1919.

49. Thomas, H. M.: Rupturing Encapsulated Empyema Into the Pleural Cavity, *J. A. M. A.* **72**:29 (Jan. 4) 1919.

50. Patterson, E. J.: Peanut Bronchitis, *New York M. J.* **109**:101 (Jan 18) 1919.

body origin is unsuspected. Occasionally, after bronchoscopy, tracheotomy is necessary to prevent a child dying in his own secretions. Bowen⁵¹ stresses the same point. For a variety of reasons, unsuspected foreign bodies in the lungs are of frequent occurrence in children, much more frequent than previous experience has indicated. The usual diagnosis is chronic bronchitis, less frequently it is slowly advancing tuberculosis. The average general practitioner is far too apt to discount the probability of the presence of a foreign body in the lung.

FETAL BRONCHIECTASIS

Koecker⁵² reviews the literature of the two types of congenital bronchiectasis and describes an interesting type of the fetal kind, discussing some points suggested by his own case. The cause of fetal bronchiectasis is unknown, but its bronchial origin cannot be doubted. Among modern investigators the current belief is that it is a primary maldevelopment.

ASTHMA

Scheppegrell⁵³ states that 5 per cent. of hay-fever cases develop before the age of 5 years, and 24 per cent. before the age of 24 years. It is relatively common among children, but it is not recognized as the diagnosis is usually "a cold."

The initial sensitization of hay-fever pollen in children is usually due to the direct inhalation of certain wild flowers. A common one is the daisy fleabane, *Erigeron strigosus*, found usually in neglected fields and on roadsides. It has some resemblance to the common daisy, and is therefore frequently collected by children. Another is the common dandelion, *Leontodon taraxacum*. The pollen is quite noxious and often causes an attack of hay-fever which is usually mistaken for a cold. This is not listed on the hay-fever weed list because it is not wind pollinated.

The field daisy, black eye susan, and others of the "compositae" family are insect pollinated and thus do not infect the atmosphere for hay-fever sufferers, but if applied directly to the nostrils, and the pollen is inhaled, an anaphylaxis may develop, resulting in a sensitization to other members of the same group. As ragweed is a "compositae," the sensitization may result in a persistent fall hay-fever.

Initial attacks are usually due to increased exposure; these are followed by an anaphylaxis to atmospheric pollens which previously failed to produce an attack.

51. Bowen, D. R.: The Unsuspected Foreign Body as a Frequent Cause of Chronic Bronchitis, *Am. J. Roentgenol.* **6**:111 (March) 1919.

52. Koeckert, H. L.: Fetal Bronchiectasis, *Am. J. Dis. Child.* **17**:95 (Feb.) 1919.

53. Scheppegrell, W.: Hayfever in Children, *Med. Rec.* **96**:97 (July 19) 1919.

As in adults, asthma is sometimes the predominant symptom of hay-fever in children. When asthma is marked during the hay-fever season, the reaction to pollens is probable. The treatment is outlined and the results of this have been very encouraging.

Donelly,⁵⁴ discussing the etiology, symptomatology and treatment of bronchial asthma in children, calls attention to the fact that in the sensitization tests there is a marked reaction, in a large percentage of cases, to the protein of walnut, and he believes that not enough attention has been given to this point. Walker's⁵⁵ conclusions, following his studies on the treatment of asthma with vaccines, are as follows: Twenty-eight patients with bronchial asthma were treated with vaccines of the bacteria to which they were sensitive. Seventy-five per cent. were relieved of asthma and 21 per cent. were improved. Seventy-five patients were treated with vaccines made from culturing their sputum on plain agar. The predominating organism was usually the one selected for treatment. Forty-six per cent. were relieved of asthma and 16 per cent. were improved. These were all nonsensitive patients. Twenty-four patients were treated with vaccines made from culturing their sputum on dextrose bouillon and using only the streptococci. Thirty-seven per cent. were relieved of asthma and 25 per cent. were improved. These were also nonsensitive patients. Sixteen nonsensitive summer asthmatics were treated with vaccine. Thirty-one per cent. were relieved and 25 per cent. were improved. Thirty-five nonsensitive patients were treated by vaccines made by culturing their sputum both ways; in other words, many types of vaccines were used. Thirty-one per cent. were relieved and 23 per cent. were improved. With the sensitive cases, the age of onset of asthma, the duration of the asthma and the age of the patient when treated, had little to do with the prognosis. However, with the nonsensitive cases these facts had much bearing on the prognosis. The older a patient is when an asthma begins, and the older he is when treatment is begun, the more unfavorable the prognosis from vaccines in nonsensitive cases. Therefore, in general, the younger a patient is when asthma begins the better the prognosis, and in children the prognosis is good.

Walker⁵⁶ states further that patients who have seasonal bronchial asthma caused by pollens are prevented from having asthma by a series of treatments with the pollens to which they are sensitive, provided sufficient treatment is given. Treatment with pollens during the season is less reliable.

54. Donnelly, W. H.: *Bronchial Asthma in Children*, New York M. J. **109**: 503 (March 22) 1919.

55. Walker, I. C.: *The Treatment of Bronchial Asthma with Vaccines*, Arch. Int. Med. **23**:220 (Feb.) 1919.

56. Walker, I. C.: *Sensitization and Treatment of Asthmatics with Pollens*, Am. J. M. Sc. **157**:409 (March) 1919.

The intestinal tract is considered by Lewis⁵⁷ the "fons et origo mali." Poisons produced there are carried through the body, react on the nervous system in some way and produce the asthmatic attack. The treatment is to modify the diet so as to prevent the formation of poisons.

Brown⁵⁸ divides asthmatics into two groups—the first having definite pulmonary signs, and the second, in which there is nothing more than a transient obstacle to respiration, with little or no secretion in the bronchial tree. The first group is further divided into two sub-groups, one in which no nasal deformity or disease of the accessory sinuses exists, and a second in which one or both are present.

The original second group is likewise further divided into three subdivisions—the first, in which the nervous element is a causative factor, the second he refers to as a nasal reflex asthma, and a third in which there is no irritable nasal condition present, but there is a definite respiratory circulatory reflex.

Lorie⁵⁹ operated in thirty-nine cases of asthma and obtained thirty-five cures. He believes in the most thorough examination of the nasal passages of all cases of asthma. The case of a twelve-year-old girl is cited, who had asthma since childhood. The tonsils and adenoids were removed without any improvement. Examination finally revealed a nonsuppurating ethmoiditis. Operation resulted in a complete cure.

Sawtelle,⁶⁰ on the other hand, says that the extravagant claims for the cure of bronchial asthma by intranasal surgery alone are unsupported by scientific investigation and careful clinical observation.

RETROPHARYNGEAL ABSCESS

Ninety-six per cent. of these abscesses begin before the sixth year, and 50 per cent. occur in children between the ages of 6 months and 1 year, according to Brown.⁶¹ The diagnosis presents some difficulties to the general practitioner, as only one of the cases reported was correctly diagnosed.

These patients usually have some history of a nasopharyngeal infection, or some illness which can be traced to an infection of the upper respiratory tract. The primary condition may have been entirely recovered from or may have merged into the symptoms presented by

57. Lewis, P.: Asthma, Med. Press **107**:160, 1919.

58. Brown, R. G.: Asthma from the Point of View of the Rhinologist, M. J. Australia **2**:463 (Dec. 7) 1918.

59. Lorie, A. J.: Nasal Sinuses and Asthma, J. Missouri M. A. **16**:113 (April) 1919.

60. Sawtelle, J. E.: The Relation of Focal Infection and Protein Poisoning to the Upper Respiratory Tract, J. Kansas M. S. **19**:25 (Feb.) 1919.

61. Brown, J. M.: Acute Retropharyngeal Abscesses in Children, Laryngoscope **29**:9 (Jan.) 1919.

the retropharyngeal abscess. As the abscess develops, there is a return of the fever or an increase in that which was already present, together with general symptoms that accompany any infectious process.

The local symptoms are some interference with respiration and deglutition. Because of this, many cases are diagnosed croup. The dyspnea is usually inspiratory in type, this being one of the best diagnostic symptoms. Choking spells are common; the child almost strangles, and in one of the cases reported tracheotomy had to be done to restore breathing. Any child having trouble with respiration and deglutition should be regarded as a possible subject of a retropharyngeal abscess, and, if necessary, a digital examination of the pharynx should be made.

He regards it as a very serious lesion if undiagnosed, and does not believe in allowing spontaneous rupture. One of the patients whose case is reported undoubtedly choked to death following a spontaneous rupture, the small larynx having been filled with pus during a sudden inspiration.

The only rational treatment, Marfan⁶² says, is operation, and this should be done immediately. The inside method is much preferred.

ROENTGEN RAY IN THE DETECTION OF FOREIGN BODIES

Jackson⁶³ has an excellent résumé of cases of foreign bodies in the air passages, presenting particularly the pathology of different types. Bowen⁶⁴ reporting the case of a boy, aged 8 years, who had had a foreign body in his lungs for five years, pleads for the use of the roentgen ray in routine examination of the thorax, if for no other reason than to eliminate the question of foreign body.

PHYSIOLOGY

Meakins⁶⁴ applies lessons learned while investigating respiratory disturbances due to gas irritation, to those occurring in civil practice. Pneumonia dyspnea, he believes, is due to an oxemia primarily, and the usual method of treating the dyspnea, associated with cyanosis and vasomotor paralysis, with oxygen is all wrong. The oxygen must be used intelligently, and the proper way is that devised by Haldane, involving the use of a mask.

The significance of Hoover's⁶⁵ observations lies in the recognition of disassociation between anoxemia and carbon dioxid of the blood.

62. Marfan: *Acute Retropharyngeal Abscess*, Med. Press **1**:468, 1918.

63. Jackson, C.: *Observations on the Pathology of Foreign Bodies in the Air and Food Passages*, Surg., Gyn. & Obst. **28**:201 (March) 1919.

64. Meakins, J. C.: *Causes and Consequences of Disturbances of Respiratory Rate and Rhythm*, Canadian M. A. J. **9**:319 (April) 1919.

65. Hoover, C. F.: *Moisture in the Air Spaces of the Lungs and Oxygen Therapy*, Tr. Sect. Pharmacol. & Therap., A. M. A., p. 103, 1918.

Unless the entire volume of blood passing through the pulmonary circulation is exposed to a respiratory membrane which has a uniform exposure to the ventilating air of the lungs, the analyses of expired air cannot be employed to interpret the oxygen and carbon dioxide content of the blood.

MISCELLANEOUS

Bennett ⁶⁶ insists that the purity and not the coldness of the air is the *sine qua non* of respiratory treatment. He believes that many of the recently published opinions against the use of alcohol in pneumonia are brought about, partly, at least, by the present wave of prohibition. Coal tar products are taboo, and pneumonia patients are rarely examined, once the diagnosis is made.

Analyzing some of the facts relating to the frequency of acidosis in children, Stevens ⁶⁷ believes that infection of the upper respiratory passages may be an etiologic factor. A preliminary survey of several cases, treated with that viewpoint in mind, were presented.

Osborne ⁶⁸ calls attention to the fact that colds, especially in children, are to be considered regrettable occurrences and should always be treated properly and never neglected. He suggests the use of $\frac{1}{500}$ grain atropin for a child 10 years old, only, however, in the early stages of the disease. This is to be given every three hours, for five doses, then every six hours, for five more doses. This is a valuable adjunct in addition to other methods which he describes.

An excellent discussion of ventilation is given by Reed ⁶⁹ with a good bibliography. In his summary he states that because the effects of fatigue are now recognized as being similar to those caused by poor ventilation, it is apparent that there is a close relationship between the two conditions, and it may be that the effects are the same though the mechanism is not clearly outlined.

Pulmonary syphilis ⁷⁰ is seldom diagnosed until necropsy. The chief forms are: gumma, bronchiectasis and pneumonia.

66. Bennett, C. D.: *The Cult of Cold*, J. M. Soc. New Jersey **16**:84 (March) 1919.

67. Stevens, F. A.: *Acidosis and Its Relations to Upper Respiratory Conditions*, J. Iowa S. M. S. **8**:136 (April) 1919.

68. Osborne, O. T.: *The Etiology and Treatment of Colds*, New York M. J. **109**:529 (March 29) 1919.

69. Reed, C. I.: *Why Is Poor Ventilation Harmful?* Am. J. Pub. Health **9**:589 (Aug.) 1919.

70. Canelli, A. F.: *Congenital Pulmonary Syphilis*, La Pediatria **27**:11 (Jan.) 1919.

American Journal of Diseases of Children

VOL. 19

APRIL, 1920

No. 4

INFANT AND CHILD MORTALITY

INCLUDING MISCARRIAGES AND STILLBIRTHS *

HERMAN SCHWARZ, M.D.
NEW YORK

The material for this work is taken from the social histories of 10,000 families which we have gathered in the course of ten years. The social status represented is that usually seen in a large city such as New York, in families in which the earning capacity in prewar times was from ten to eighteen dollars a week, a bare living wage. The nationalities included are approximately:

	Per Cent.
Americans (born in the United States).....	17
Russian Jews, native and foreign born.....	40
Austro-Hungarians	22
Negroes	5
Italians	5
Miscellaneous	11

We were fortunate in having, during the period covered, the same social worker, a woman versed in the various languages, so that the data may be considered fairly even and accurate. The social histories were obtained on special cards,¹ on which were noted income, nationality, pregnancies, miscarriages, etc. Of the 10,000 charts of social histories thus obtained, we have analyzed only the first 7,000, partly on account of the stupendous amount of work involved, and also because we believe that the present moment — when all the belligerent nations are anxious to do everything possible for the welfare of the coming generation — is an opportune time to publish some of our figures. We hope that any information which we have gathered may be of some value.²

Table 1 gives a general survey of the scope of this contribution to the study of infant mortality. In 6,968 families there were 27,711

* A statistical report from the Pediatric Department of the John E. Berwind Maternity Clinic.

1. See first annual report of the clinic published in 1908.

2. In order to make the tables as easily understood as possible, we would note that "total pregnancies" means all the pregnancies, including live born miscarriages and stillbirths. Living births refers to those pregnancies which resulted in live born infants.

pregnancies, including miscarriages and stillbirths, an average of 3.9 per family. Of these 27,711 pregnancies, 2,239 were miscarriages and 413 were stillbirths, the remainder, or 25,059, represent the number of living births; that is, there were 3.6 live born children to each family. The total number of deaths under 1 year of living births were 3,232. From the first to the eighth year there were 1,081 additional deaths, or a total of 4,313 deaths of living births. Taking all the deaths up to 8 years, including miscarriages and stillbirths, we find that of the 27,711 pregnancies, 6,965 babies, or 25 per cent., died; that is, wasted:

TABLE 1.—RESULTS OF GENERAL SURVEY OF INFANT MORTALITY

Number of families.....	6,968	
Number of pregnancies (miscarriages and stillbirths included).....	27,711	
Number of miscarriages.....	2,239	
Percentage of miscarriages to total pregnancies.....		8.07
Number of stillbirths.....	413	
Percentage of stillbirths to total pregnancies.....		1.49
Total deaths under 1 year of living births.....	3,232	
Percentage of infantile deaths to total pregnancies.....		11.66
Percentage of infantile deaths to living births.....		12.89
Total deaths of infants and children up to 8 years.....	4,313	
Percentage of child deaths up to 8 years to total pregnancies.....		15.56
Percentage of child deaths up to 8 years to living births.....		17.21
All fatalities—deaths, stillbirths, miscarriages.....	6,965	
Percentage of all fatalities to total pregnancies.....		25.13
Miscarriage rate.....	80.7 per 1,000 (total) pregnancies	
Miscarriage rate.....	89.3 per 1,000 living births	
Stillbirth rate.....	14.9 per 1,000 (total) pregnancies	
Infant death rate.....	116.6 per 1,000 (total) pregnancies	
Infant death rate.....	128.9 per 1,000 living births	
Child death rate (to 8 years).....	155.6 per 1,000 (total) pregnancies	
Child death rate (to 8 years).....	172.1 per 1,000 living births	
Total fatalities rate.....	251.3 per 1,000 (total) pregnancies	

TABLE 2.—NUMBER OF PREGNANCIES PER FAMILY

Number of Families in Series	Number of Pregnancies per Family	Total Number of All Pregnancies	Number of Families in Series	Number of Pregnancies per Family	Total Number of All Pregnancies
1,057	1	1,057	57	11	627
1,276	2	2,552	43	12	516
1,177	3	3,531	15	13	195
1,029	4	4,116	16	14	224
779	5	3,895	5	15	75
607	6	3,642	4	16	64
495	7	2,835	3	17	51
239	8	1,912	3	19	57
168	9	1,512			
85	10	850	6,968		27,711

an entire economic loss. Unfortunately, our statistics cannot be used to total the amount of loss up to the working age in order to find out the real economic loss to the nation. Computing rates in terms of a thousand pregnancies, we find that the miscarriage rate in these families was 80.7 per thousand of all pregnancies and 89.3 per thousand of living births. The infant death rate (up to 1 year of age) in this group of families was 128 per thousand living births. A contrast to this figure is the death rate of 70 per thousand in this same group of families of only those of their children who, during the ten years,

were under our care. This figure, which shows a saving of 58 infants per thousand living births, proves conclusively what supervision, education and care can accomplish. The child death rate (up to eight years) reached 172 per thousand. In other words, 172 out of every thousand children born alive, died before they reached the age of 8 years.

TABLE 3.—AVERAGE NUMBER OF MONTHS BETWEEN PREGNANCIES

Number of Families in Series	Number of Pregnancies per Family	Total Number of Pregnancies	Average Number of Months between Pregnancies
1,276	2	2,552	15
1,177	3	3,531	19
1,029	4	4,116	22.5
779	5	3,895	22.5
607	6	3,642	23
495	7	2,855	22
239	8	1,912	21
168	9	1,512	21
85	10	850	20.5
57	11	627	18
43	12	516	20
15	13	195	19
16	14	224	16.5
5	15	75	15
4	16	64	13
3	17	51	13.5
3	19	57	12.5
5,911		26,654	20

In Table 3 we have tried to show how frequently pregnancy occurs in these families. As the marriage date was not available in our data, and the length of marriage thus impossible to obtain, we computed the months between the various pregnancies from the date of the termination of the first pregnancy. It will be seen that the average interval between pregnancies, in families with from four to six pregnancies, is twenty-two and a half months, and in families with from two to ten pregnancies the average interval is never less than twenty months. Even among these families there is not a child born every year. From this standpoint it might not be inappropriate to say a word concerning the declining birth rate. Since so much vicious propaganda has been going on in all countries about birth control I cannot do better than to refer to Louis I. Dublin's address as retiring vice president of the American Association for Advancement of Science, read at Pittsburgh, Dec. 29, 1917, Section I, Social and Economic Science. He showed that at the beginning of the nineteenth century, France had a population of 29,000,000; Germany a population of 23,000,000, and England and Wales a population of 18,000,000. At the beginning of the twentieth century the facts were almost reversed. Germany's population was 65,000,000; England and Wales, 45,000,000, and France 39,000,000. In 1860, France was still in the lead with a population of 37,000,000; from 1860 to 1914 it increased only 2,000,000. This was in part due to

decreased birth rate, but also to a high infantile death rate. In 1830, the birth rate in France was 30 per thousand; in 1914 it was 18 per thousand, and the infantile death rate was 19.6 per thousand—the death rate exceeding the birth rate. To show, as Mr. Dublin does so well, how this shifts the population, it might be interesting to know that in Germany, one quarter of the population was less than 11 years of age; in England and Wales, one quarter of the population was less than 12 years of age; in France, one quarter of the population was less than 14 years of age. In Germany, three quarters of the population was less than 41 years of age; in England and Wales, three quarters of the population was less than 42 years of age, and in France, three quarters of the population was less than 49 years of age. In the United States, although our statistics are not very accurate, the birth rate is probably 25 per thousand, and the death rate 15 per thousand, a yearly increase of about 1 per cent. to our population.

TABLE 4.—INCIDENCE OF MISCARRIAGE

Total Number of Families in Series	Number of Pregnancies per Family	Number of Families in which Miscarriage Occurred	Total Number of Miscarriages	Total Number of All Pregnancies	Miscarriages per Thousand of All Pregnancies
1,957	1	0	0	1,057	0.0
1,276	2	93	94	2,552	36.8
1,177	3	155	162	3,531	45.8
1,029	4	209	260	4,116	63.4
779	5	225	283	3,895	72.6
607	6	222	306	3,642	83.4
405	7	158	257	2,835	91.0
239	8	125	231	1,912	120.8
168	9	110	211	1,512	139.5
85	10	55	120	850	141.2
57	11	34	71	627	113.2
43	12	33	78	516	151.1
15	13	14	46	195	235.8
16	14	12	40	224	178.5
5	15	5	23	75	306.6
4	16	4	20	64	312.5
3	17	3	17	51	333.3
3	19	3	20	57	350.8
6,968	..	1,460	2,239	27,711	80.7

Percentage of miscarriages to total pregnancies, 8.07.

Percentage of miscarriages to living births, 8.92.

It may be asked, "How large must a family be in order to keep our population from diminishing?" In order to have an individual born, there certainly must be two others alive. If we take 100,000 individuals at birth, only 73,000 (Dublin) are alive at the age of marriage,³ so that at least two and one half individuals are necessary to produce another individual. At least from 12 to 15 per cent. of these 73,000 do not marry, and 7 per cent. of those who do marry have no children, so that from three and one half to four individuals must be born to insure a new individual.

3. According to our figures many less than this are alive at the marriageable age.

In 6,968 families with 27,711 pregnancies, including living births, miscarriage and stillbirth pregnancies, there were 2,239 miscarriages, a rate of 80.7 per thousand, or 8 per cent. of all the pregnancies. This miscarriage rate is in direct proportion to the number of pregnancies in the family. With two pregnancies per family, the rate was 36.8 per thousand; with three pregnancies, it was 45.8 per thousand, and so on, until in eighty-five families with ten pregnancies, the rate was 141.2 per thousand, more than 10 per cent. of all the pregnancies ending in miscarriages. Of the 850 pregnancies in families with more than ten pregnancies per family, the number is really too small to make any definite statement, yet it is interesting to see, from what material we have, how great the fetal death rate is. For instance, in sixteen families with fourteen pregnancies each, i. e., 224 pregnancies, there were forty miscarriages, or 17 per cent. In four families with sixteen pregnancies each, the fetal death rate was 30 per cent.

TABLE 5.—INCIDENCE OF STILLBIRTHS

Total Number of Families in Series	Number of Pregnancies per Family	Number of Families in which Stillbirths Occurred	Total Number of Stillbirths	Total Number of All Pregnancies	Stillbirths per Thousand of All Pregnancies
1,057	1	0	0	1,057	0.0
1,276	2	22	22	2,552	8.6
1,177	3	42	45	3,531	12.7
1,029	4	48	51	4,116	12.3
779	5	59	63	3,895	18.9
607	6	46	58	3,642	15.9
405	7	35	43	2,835	15.2
239	8	32	43	1,912	22.4
168	9	17	25	1,512	16.5
85	10	23	26	850	30.5
57	11	19	18	627	27.5
43	12	6	12	516	23.2
15	13	3	6	195	30.7
16	14	0	0	224	0.0
5	15	1	1	75	13.3
4	16	0	0	64	0.0
3	17	0	0	51	0.0
3	19	0	0	57	0.0
6,968	..	342	413	27,711	14.9

Percentage of stillbirths to total pregnancies, 1.49.

Percentage of stillbirths to living births, 1.64.

The stillbirth rate per thousand total pregnancies was 14.9, and per thousand living births it was 16.4. This is much lower than that for New York City, which, according to Dr. Guilfoyle,⁴ was from 43 to 49 per thousand births during the past five years. The same condition as in the miscarriage rate exists here also, the rate going up steadily in direct proportion to the number of pregnancies in the family. With two pregnancies per family, the rate was 8.6 per thousand of all pregnancies; with ten pregnancies per family, the rate was 30.5 per thousand. The total still birth rate is about 14.9 per thousand preg-

4. Personal communication to the author

nancies, or 1.49 per cent. This is more than the stillbirth rate in the various cities, but I believe it to be more accurate, for many stillbirths are undoubtedly not reported.

Table 6 gives a very good idea of the relation of the infant mortality rate to the entire pregnancy rate and to the "living births" rate, if I may use that term. Here, again, there is a direct relationship between the number of pregnancies of all kinds and also the number of living births to the infant mortality rate. With two pregnancies in the family, the rate is 75.1 and 78.4 per thousand, respectively, whereas with ten pregnancies, the rate is 174.1 and 210.2 per thousand. Families with a greater number of pregnancies are interesting only from the standpoint of the greater death rate present. The average infant mortality rate in all of our families was 116.6 per thousand for all pregnancies, and 128.9 per thousand for living births, whereas, under the same living and social conditions, but under the supervision of our clinic, the death rate for living births in these families has never been more than 70 per thousand.

TABLE 6.—DEATHS OF LIVE BORN INFANTS FROM BIRTH TO ONE YEAR OF AGE. INFANT MORTALITY

Total Number of Families in Series	Number of Pregnancies per Family	Number of Families in which Death Occurred (Birth-1 Year)	Total Number of Deaths of Infants	Total Number of All Pregnancies	Deaths per Thousand of All Pregnancies	Total Number of Living Births	Deaths per Thousand of Living Births
1,057	1	57	57	1,057	53.9	1,057	53.9
1,276	2	177	191	2,552	75.1	2,436	78.4
1,377	3	275	314	3,531	88.9	3,324	91.7
1,029	4	308	372	4,116	90.3	3,805	97.7
779	5	310	413	3,895	106.0	3,549	116.3
607	6	314	471	3,642	129.3	3,278	143.9
405	7	246	375	2,843	132.2	2,535	143.9
239	8	149	267	1,912	139.6	1,638	162.6
168	9	119	245	1,512	162.0	1,276	192.7
85	10	66	148	850	174.1	704	210.2
57	11	48	137	627	218.5	538	254.6
43	12	35	102	516	199.8	426	239.4
15	13	13	26	195	133.3	143	181.8
16	14	16	61	224	272.4	184	331.5
5	15	4	13	75	173.3	51	254.9
4	16	3	16	64	250.0	44	363.6
3	17	3	18	51	352.9	34	529.4
3	19	2	6	57	105.2	37	162.1
6,968	..	2,145	3,232	27,711	116.6	25,059	128.9

Percentage of infant deaths to total pregnancies, 11.66.
Percentage of infant deaths to living births, 12.89.

Table 7 shows still better what happens to children in these families, especially in relation to the number of children in the family. With two and three pregnancies the table does not really describe conditions accurately, for many of the children born had not reached the age of 8 years. However, in going up the scale, it will be seen that with five pregnancies per family the death rate is 162.8 per thousand, or 16 per cent. of all the children born alive never reach the age of 8 years

With ten pregnancies, 29 per cent. of those born alive succumb before reaching the eighth year. There were 25,059 living births with 4,313 deaths, a mortality of 17 per cent. Of these deaths, 3,232 occurred during the first year and 1,081 children died between the first and the eighth year.

TABLE 7.—DEATH OF CHILDREN FROM BIRTH TO EIGHT YEARS OF AGE

Total Number of Families in Series	Number of Pregnancies per Family	Number of Families in which Death Occurred (Birth-1 Year)	Total Number of Deaths of Children	Total Number of All Pregnancies	Deaths per Thousand of All Pregnancies	Total Number of Living Births	Deaths per Thousand of Living Births
1,057	1	57	57	1,057	53.9	1,057	53.9
1,276	2	200	213	2,552	83.4	2,436	87.4
1,177	3	331	378	3,531	104.3	3,324	113.7
1,029	4	407	502	4,116	121.9	3,805	131.9
779	5	113	578	3,895	148.4	3,549	162.8
607	6	393	644	3,642	177.4	3,278	196.4
405	7	294	523	2,835	184.4	2,535	206.3
239	8	182	377	1,912	171.5	1,638	209.2
168	9	137	328	1,512	216.9	1,276	257.0
85	10	73	205	850	241.1	704	291.1
57	11	53	190	627	303.0	538	363.1
43	12	43	139	516	269.3	426	326.2
15	13	14	36	195	184.6	143	251.7
16	14	16	74	224	375.0	184	402.1
5	15	5	16	75	213.3	51	313.7
4	16	4	19	64	296.8	44	431.8
3	17	3	23	51	450.9	34	655.8
3	19	2	11	57	192.9	37	297.1
6,968	..	2,627	4,313	27,711	155.6	25,059	172.1

Percentage of total deaths of children up to 8 years to total pregnancies (miscarriages and stillbirths), 15.56.

Percentages of total deaths of children up to 8 years to living births, 17.21.

TABLE 8.—ALL FATALITIES—DEATHS, MISCARRIAGES, STILLBIRTHS—IN FAMILIES UP TO EIGHT YEARS

Total Number of Families in Series	Number of Pregnancies per Family	Number of Families in which Fatalities Occurred	Total Number of Fatalities	Total Number of Pregnancies	Fatalities (Living Births, Miscarriages and Stillbirths per Thousand of All Pregnancies)
1,057	1	57	57	1,057	53.9
1,276	2	298	329	2,552	128.9
1,177	3	487	585	3,531	165.6
1,029	4	570	813	4,116	197.5
779	5	537	924	3,895	237.2
607	6	475	1,008	3,642	277.0
405	7	342	823	2,835	290.3
239	8	216	651	1,912	340.4
168	9	167	564	1,512	373.0
85	10	78	351	850	412.9
57	11	57	279	627	447.9
43	12	43	229	516	443.7
15	13	15	88	195	451.2
16	14	16	114	224	508.9
5	15	5	40	75	533.3
4	16	4	39	64	609.3
3	17	3	40	51	784.3
3	19	3	1	57	80.4
6,968	..	3,383	6,083	27,711	219.2

Percentages of all fatalities to all pregnancies, 25.12.

TABLE 9.—[INFANT AND CHILD MORTALITY (UP TO EIGHT YEARS) IN RELATION TO THE NATIONALITY OF THE PARENTS.
MATERIAL: 5,968 FAMILIES; 26,711 PREGNANCIES]

[illegible]

MISCARRIAGE RATE TO ALL PREGNANCIES AND LIVING BIRTHS
UP TO THE EIGHTH YEAR

UP TO THE ENGLISH DEATH		DEATHS PER THOUSAND LIVING BIRTHS		UP TO THE ENGLISH DEATH		DEATHS PER THOUSAND LIVING BIRTHS	
PREGNANCIES		PREGNANCIES		PREGNANCIES		PREGNANCIES	
PREGNANCIES		PREGNANCIES		PREGNANCIES		PREGNANCIES	
Both parents born in the U. S. A.	104.9	119.4	342.8	34	342.8	34	342.8
Father born in the U. S. A.	76	85.7	307.8	30.7	307.8	30.7	307.8
Mother born in the U. S. A.	62.8	80.7	280.7	28.0	280.7	28.0	280.7
Both parents of foreign birth.	79.9	86.2	240	24	240	24	240
Colored group.	116	135.8	320.5	32	320.5	32	320.5

STILLBIRTH RATE TO ALL PREGNANCIES AND LIVING BIRTHS
UP TO THE EIGHTH YEAR

Deaths per Thousand and Pregnancies		Deaths per Thousand and Living Births	
Total	Living Births	Total	Living Births
17.4	19.7	251.2	251.2
57.1	30	206	210
12.1	18.6	133.4	133.4
13.2	15.2	192.7	192.7
23.5	34.3	142.4	142.7
		175	204

TABLE 10.—FATALITIES IN RELATION TO LITERACY OF PARENTS UP TO EIGHT YEARS. MATERIALS 5,908 FAMILIES; 26,711 PREGNANCIES

Num- ber of Fam- ilies	Total Number of Preg- nancies	Number of Living Births	Num- ber of Deaths of Living Births	Deaths of Living Births per Thou- sand Total Preg- nancies	Miscar- riage Rate per Thou- sand Total Preg- nancies	Miscar- riage Rate per Thou- sand Living Births	Num- ber of Still- births	Still- birth Rate per Thou- sand Total Preg- nancies	Still- birth Rate per Thou- sand Living Births	Num- ber of Total Fetal- ities	Total Death per Thou- sand Total Preg- nancies	Total Death per Thou- sand Living Births
One or both parents literate.....	4,897	22,298	20,050	3,513	125.3	85.5	342	15.3	17	5,761	958	175.2
Both parents illiterate.....	966	3,870	3,513	713	203.1	75.1	66	17	18.7	1,070	276.4	202.9

FATALITIES OF ALL PREGNANCIES UP TO THE EIGHTH YEAR				MISCARRIAGE RATE			
One or both parents literate.....	One or both parents illiterate.....	Deaths per Thousand Living Births	Deaths per Thousand Total Pregnancies	One or both parents literate.....	One or both parents illiterate.....	Miscarriages per Thou- sand Living Births	Miscarriages per Thou- sand Total Pregnancies
.....	17.5%	25.8%	85.5	95.4
.....	20.3%	27.6%	75	82.4

FATALITIES OF LIVING BIRTHS UP TO THE EIGHTH YEAR				STILL BIRTH RATE			
One or both parents literate.....	One or both parents illiterate.....	Deaths per Thousand Living Births	Deaths per Thousand Total Pregnancies	One or both parents literate.....	One or both parents illiterate.....	Stillbirths per Thou- sand Living Births	Stillbirths per Thou- sand Total Pregnancies
.....	11.2%	12.5%	15.3	17
.....	18.4%	20.3%	17	18.7

Table 8 shows all fatalities in these families up to 8 years. Here, again, the relationship to the number of pregnancies is apparent, and, in addition, the important economic fact is shown that 25 per cent. of all the conceptions have been for naught before first eight years of life are passed.

The nationality of the parents in relation to infant and child mortality is perhaps a minor factor, for poverty, housing conditions and literacy all form a part of the great cause of child mortality. Yet, it is the common experience of those who have worked among the poor to find that the native born who have been content to remain in the slums do so because they are often a very shiftless group, and who, above all, either do not seem to have the ability or the desire to nurse their children. The death rate, in early infancy, of children of native born parents, greatly exceeds that of the foreign element. It is well known that the nursing infant is fairly immune to its surroundings as long as it is kept on the breast. Thus, the figures for total fatalities of 342, 307 and 289 per thousand pregnancies of native born parents, as compared with 240 per thousand born of foreign parents, are not surprising. The fatalities in the live born children are just as marked. This also seems to hold good in other strata of society, for in the 1916 census of the births and deaths in the registration area the same thing is observed. The colored group, curiously enough, shows less total fatalities than in the group in which both parents (white) were born in the United States. The number of our colored families is too small, however, to make satisfactory comparisons.

The miscarriage rate is greatest when both parents are native born and least when both parents are foreign born. The colored group, as was to be expected, shows the largest number of miscarriages, owing, no doubt, to the great amount of syphilis present.

The stillbirth rate is made up of so few cases that it is best not to draw any deductions.

The relation of infant and child mortality to the literacy of the parents is always interesting, but very difficult to make convincing. That parents who are literate are apt to have a more systematic and well regulated household there can be no doubt; that literacy tends to a clearer comprehension of the instructions given and thus an increased knowledge of infant and child welfare, there is no question. Yet shiftlessness and drunkenness can very well go along with literacy. However, literacy in the parents does place them on a little higher plane of civilization than illiteracy. The table shows very nicely the difference in the two classes, and very much in favor of literacy.

The summaries of Table 10 show that of the deaths of living births, the rate for literacy is 112.5 to 125.3 as compared with 184 and 203.1, respectively, for illiteracy. In the miscarriage rate, however, the con-

ditions are reversed, for the literate have more miscarriages than the illiterate. In the stillbirth rate, the figures are about the same, which might be expected. In a previous tabulation⁵ we showed a similar condition, but with fewer families. There were 358 literate families with an infantile mortality rate of 111 per thousand born, and 113 illiterate families with an infant mortality rate of 172 per thousand born. It does seem that education is a very important factor.

We wish to thank Dr. I. L. Hill and Mr. John E. Berwind for the hearty cooperation and advice which they have given us.

5. First Annual Report of the John E. Berwind Maternity Clinic.

RESULTS OF SOME EXPERIMENTAL WORK WITH SODIUM CACODYLATE ON ATHREPTIC INFANTS

FLOYD S. CLARKE, M.D., AND ANDREW DOW, M.D.

OMAHA

The physician is rather frequently confronted with a type of infant, who, because of some nutritional disturbance, either fails to gain in weight, or the gain is so slight as to be almost negligible.

This condition of insufficient nutrition is sometimes called athrepsia. The condition is prevalent in hospitals or institutions where many babies are housed. However, it is not uncommon in private practice and among the well-to-do. Its occurrence is much more frequent in the artificially fed infant, although it may be encountered occasionally in the breast fed.

One member of this class of infants will take its food well, does not vomit and there is no indication of digestive disturbance. The food may be of sufficient caloric value. Another member of this class of cases, will tolerate only a certain amount of food. In feeding these infants, one has to be extremely careful not to overtax this food tolerance. They are particularly unable to digest any normal amount of fat. If one exceeds their food tolerance, there occurs a definite gastrointestinal upset, with vomiting, usually a diarrhea and more rapid loss of weight.

There is in both types of cases, an inability to assimilate food properly, so as to make a normal gain in weight, in spite of careful regime as to food, time and regularity of feeding.

Careful manipulation of the food, even resorting to breast feeding, makes very little, if any, change in the infants. They do not do well. They are below par physically, anemic, and compare very unfavorably with normal, healthy infants of the same age.

In groping about for a possible solution of this problem, it seemed to one of us that the administration of arsenic to these infants might so improve them physically as to enable them to take on more weight. Spencer L. Dawes and H. C. Jackson, in a series of experiments on dogs and rabbits, concluded that after the injection of sodium cacodylate, arsenic, in inorganic form, makes its appearance in the tissues of the body. The animal body possesses the power to reduce or decompose the organic arsenic compound, sodium cacodylate, into the inorganic active arsenous or arsenic acid. Cacodyl or some of its salts are also found in the tissues after injections of sodium cacodylate, but they are of little or no therapeutic value. It is admitted that a

considerable quantity of the inorganic arsenic is eliminated by the urine, and probably by the sweat and breath; but enough is retained to have some effect therapeutically.

In their experiments, Dawes and Jackson note that almost invariably after injections the patient gains in weight. In anemic cases the percentage of hemoglobin is always increased. Arsenic exerts a tonic effect, the nutrition improving, and even in health the individual taking it in carefully graduated doses, takes on more flesh, and is not fatigued readily.

In endeavoring to come to some conclusion in this class of cases six infants were selected for study. They were all institution babies. The oldest child had been in the institution one year. Of the others, two children had been in for five months, two for six months, and child one for four months. They were all very much under weight and more or less anemic. They were all athreptics.

Before beginning the injections, a von Pirquet was done on each one with negative results. A blood Wassermann from each infant proved negative. A routine urine examination yielded similar negative results.

Regarding the diet: One child was taking cooked cereals, broths, toast, cooked vegetables, custards, jellies and about one pint of milk in twenty-four hours. Two children were taking a modified milk formula of about the same caloric value. One child was taking breast milk exclusively. One was on partial breast milk and modified milk; one was taking buttermilk with approximately a 10 per cent. corn syrup. Those children taking a bottle or breast were fed every three hours, seven feedings in twenty-four hours. The little girl on mixed diet was fed four times daily. The feedings were not changed during the course of the injections.

At the time of beginning injections, one child was 15 months old; two children were 9 months old; three were 6 months old.

Eight injections were given in all, at intervals of four days. All injections were given intramuscularly and hypodermically. The youngest infant received $\frac{1}{4}$ grain, as an initial dose; the oldest $\frac{3}{4}$ grain. The dosage was gradually increased till the youngest was receiving $\frac{3}{4}$ grain and the oldest 1 grain. The maximum dose at any one time was 1 grain.

A blood examination was done on all the infants before the injections were begun. A second examination was done after two injections, and a third after the last injection. The blood examination included a hemoglobin estimation, red and white cell count, together with a differential leukocyte count. The red and white cell count remained nearly uniform throughout, nor was there any marked change in the differential count. There was, however, a striking

increase in the hemoglobin in all the children. Three children showed an increase of five points; one child of ten points; one twenty points, and one twenty-five points. This increase in hemoglobin has been noted by other observers.

One child failed to gain in weight during the injections, but in the month succeeding gained 1 pound, 10 ounces. Three children gained approximately 2 pounds, and two gained $1\frac{1}{3}$ pounds. These gains have been continued since stopping the treatment. They all improved in nutrition and seemed to be more hungry for their food when feeding time arrived.

From the foregoing, it may be possible to draw the following conclusions:

1. That carefully graduated doses of sodium cacodylate, when injected hypodermically into infants, has no toxic influence.

2. The percentage of hemoglobin in the blood is uniformly increased.

3. While the series of cases is not large, all the children showed a substantial gain in weight, and one may conclude that sodium cacodylate possesses tonic properties enabling the individual athreptic infant to take on weight, and possibly enable him to assimilate his food more properly and thus improve his nutrition.

1. Handbook of Medical Science, New York, Wm. Wood & Co., **1**:636.

2. Hare's Practical Therapeutics, Ed. 16, Philadelphia, Lea & Febiger, p. 120.

3. Sollmann: Manual of Pharmacology, Philadelphia, W. B. Saunders Co., p. 617.

4. Forchheimer: Therapeutics of Internal Diseases, New York, D. Appleton & Co. **4**:248.

5. Dawes, S., and Jackson, H. C.: *J. A. M. A.* **48**:2090, 1907.

PROGNOSIS IN OPERATED CASES OF HYPERTROPHIC STENOSIS OF PYLORUS*

ALTON GOLDBLOOM, M.D., AND RALPH C. SPENCE, M.D.

NEW YORK

One hundred and sixty-three Rammstedt operations were performed for hypertrophic stenosis of the pylorus at the Babies Hospital between Jan. 1, 1915, and July 1, 1919. In this number are included cases already reported by Holt,¹ Downes² and Kerley,³ together with a number of cases not yet published. Holt made a survey of the whole subject; compared the medical with the surgical treatment, and demonstrated the superiority of the Rammstedt operation over other methods of treatment previously employed in this hospital. Downes, who performed the majority of the operations, described in detail the operative technic. Kerley reports twenty-six cases. These are included in this series. We have grouped all these cases together for the purpose of studying them from the standpoint of prognosis.

One hundred and thirty-one children recovered and thirty-two died, a mortality of 19.63 per cent. It is interesting to note, in connection with many previous observations, that 133 were boys and only 30 were girls. Of the boys, twenty-nine died, a mortality of 21.8 per cent., and of the girls, three died, a mortality of 10 per cent. These latter figures, however, are hardly significant.

The general rule followed at the hospital for the last few years, has been to operate as soon as a definite diagnosis has been made. Many of these children were in extremely bad condition on admission as a result of the prolonged vomiting, but in only one instance in the last six years has an operation been refused because of the child's condition. This baby had been vomiting for eight weeks, weighed less than 4 pounds, and lived only a few hours after entering the hospital. Deaths from inanition, three or four weeks after operation, are counted as operative deaths.

It becomes evident from a study of our series that the operation per se is, perhaps, the least important factor in the mortality. The condition of the baby at the time of operation is certainly the most important factor.

* From the Babies' Hospital, New York, N. Y.

1. Holt, L. E.: *J. A. M. A.* **68**:1517 (May 26) 1917.

2. Downes, W. A.: *Surg. Gyn. & Obst.* **22**:251 (March) 1916.

3. Kerley, G. G.: *J. A. M. A.* **72**:16 (Jan. 4) 1919.

CAUSES OF DEATH

Fourteen babies died from collapse from one to three days after operation, and five died from general peritonitis. In one of the latter cases the duodenum was known to have been opened accidentally at the time of operation. One child died of bronchopneumonia complicating whooping cough, and one child died from postoperative hemorrhage on the third day after operation. In this last case there was a definite history of bleeding in the family. The remaining eleven deaths were from marasmus and occurred in from three to twenty-five days after operation. In all cases, then, except the seven in which death was due to complications, the fatal result can definitely be attributed to a state of inanition existing at the time of operation. It is true, however, that the extra load incident to the anesthetic and to the shock of the operation contributed to the fatal termination. It is no less true, that operation in these cases offered the only chance of recovery.

TABLE 1.—DURATION OF SYMPTOM AND MORTALITY

Duration of Symptoms	Cases	Deaths	Mortality, %
1 week or less.....	20	1	5.0
1 - 2 weeks.....	28	7	18.42
2 - 3 weeks.....	33	2	6.06
3 - 4 weeks.....	24	5	20.83
4 - 5 weeks.....	19	6	31.58
More than 5 weeks.....	29	11	38.28
SUMMARY			
Under 4 weeks.....	115	15	13.04
More than 4 weeks.....	48	17	35.42

TABLE 2.—PREVIOUS FEEDING

	Cases	Deaths	Mortality, %
Breast fed.....	106	12	11.3
Artificially fed.....	57	20	35.0

In considering the factors which influence the prognosis, we have studied them under the following headings: (1) The duration of symptoms before operation; (2) the type of feeding before operation; (3) the weight at the time of operation; (4) the percentage of weight loss at the time of operation.

In Table 1 is shown the mortality in relation to duration of symptoms before operation. Since vomiting is usually the first symptom noted by the mother, we have taken this as the basis of our time divisions. As shown by this table, the mortality increased directly with the duration of symptoms, except in those children who vomited from one to two weeks before operation. Of these, thirty-one recovered and seven died, a mortality of 18.42 per cent. This is much higher than the mortality in the group in which vomiting occurred from two to three weeks before operation. In examining the records in

the seven fatal cases in this group, it was found that there were two deaths from general peritonitis and five from inanition. All of the children suffering from inanition had lost 25 per cent. or more of their weight even though their symptoms had lasted less than two weeks. Comparing these with the fatalities in the other groups it was evident that this group contained a larger proportion of severe cases.

The mortality as influenced by the type of feeding before operation is shown in Table 2. In determining the type of feeding, we have considered those artificially fed who had received no breast milk during the two weeks preceding their admission to the hospital. Infants only partially artificially fed were classed as breast fed, as also were those weaned within the two weeks preceding their admission. In these latter cases, the mothers' milk had not entirely disappeared and was often easy to reestablish.

TABLE 3.—PREVIOUS FEEDING, AND DURATION OF SYMPTOMS

	Cases	Deaths	Mortality, %
Breast Fed Babies:			
Vomiting, less than 4 weeks.....	88	9	10.2
Vomiting, more than 4 weeks.....	18	3	16.6
Artificially Fed Babies:			
Vomiting, less than 4 weeks.....	27	6	22.2
Vomiting, more than 4 weeks.....	30	14	46.6

TABLE 4.—BODY WEIGHT AT TIME OF OPERATION

Weight	Cases	Deaths	Mortality, %
5 pounds or less.....	5	2	40
5 - 6 pounds.....	32	10	31
6 - 7 pounds.....	57	14	25
7 - 8 pounds.....	45	5	11
8 - 9 pounds.....	18	1	6
More than 9 pounds.....	6	0	0
SUMMARY			
Less than 7 pounds.....	94	26	28
7 pounds and over.....	69	6	8.7

In order to determine whether the mortality based on the duration of symptoms was influenced in any way by the type of feeding, we have divided the breast and the artificially fed cases, each, into two groups which correspond to the summary of Table 1. Namely, (1) those children who had vomited less than four weeks and (2) those who had vomited four weeks and more.

A study of Table 3 shows that the mortality in the corresponding divisions is definitely lower for the breast fed infants. It is interesting to observe that the mortality of the breast fed infants who had vomited more than four weeks is lower than that of the artificially fed infants who had vomited less than four weeks.

The weight at the time of operation has always been considered a valuable guide in determining the prognosis. Table 4 shows the mortality based on this factor. The summary of Table 4 shows the enor-

mous difference in mortality between the infants weighing less than 7 pounds at the time of operation and those weighing 7 pounds and over.

The influence both of the duration of symptoms before operation and of the weight of the infant at the time of operation to the mortality is shown in Table 5. It is worthy of note, that an infant weighing 7 pounds and over who has vomited four weeks or more, has little better chance of recovery than the infant weighing less than 7 pounds who has vomited less than four weeks before coming to operation. The duration of the symptoms before operation, then, is a very important factor in influencing the mortality as well as is the weight of the infant at the time of operation.

TABLE 5.—WEIGHT AND DURATION OF SYMPTOMS

	Cases	Deaths	Mortality, %
Vomiting less than 4 weeks:			
Weight 7 pounds and more.	50	3	6.0
Weight less than 7 pounds.	65	12	18.5
Vomiting 4 weeks and over:			
Weight 7 pounds and more.	19	3	15.8
Weight less than 7 pounds.	29	14	48.2

TABLE 6.—WEIGHT LOSS AND MORTALITY

	Cases	Deaths	Mortality, %
Total Cases:			
0 to 10 per cent. loss.	26	0	0
10 to 20 per cent. loss.	50	5	10
20 to 30 per cent. loss.	39	13	33
More than 30 per cent. loss.	12	6	50
Breast Fed:			
0 to 10 per cent. loss.	15	0	0
10 to 20 per cent. loss.	33	1	3
20 to 30 per cent. loss.	28	8	28.5
More than 30 per cent. loss.	2	0	0
Artificially Fed:			
0 to 10 per cent. loss.	8	0	0
10 to 20 per cent. loss.	17	4	23.5
20 to 30 per cent. loss.	11	5	45.5
More than 30 per cent. loss.	10	6	60

Table 6 shows the mortality as influenced by the percentage of weight lost in the total number of cases, the breast fed cases and the artificially fed cases. There were 127 cases in which the actual loss in weight was known. Among these there were twenty-four deaths. In the entire group the mortality increased directly with the percentage of weight loss. This is to be expected from our findings in Table 4, which shows the mortality as influenced by the weight at the time of operation. Dividing the cases into two groups, namely, those children that had lost less than 20 per cent. of their best weight and those who had lost 20 per cent. and more of their best weight, there are in the former group seventy-six cases and five deaths, a mortality of 6.58 per cent., while in the latter group there are fifty-one cases with nineteen deaths, a mortality of 37.25 per cent.

There were eighty-one breast fed infants in the breast fed group of whom seventy-two recovered and nine died; a mortality of 11.11 per cent. There were only two breast fed infants who had lost 30 per cent. or more of their best weight; both recovered. Of course, no conclusion can be drawn from two cases. Forty-one breast fed infants came to operation who had lost less than 20 per cent. of their best weight; only one of these babies died. In this group are included the babies suffering from the milder form of this disease. Thirty breast fed infants had lost 20 per cent. and more of their best weight; eight of these died, a mortality of 26.66 per cent.

It is interesting to compare the figures of the breast fed infants in Table 6 with those of Table 3. In Table 3 there are eighty-eight breast fed infants in the group that vomited less than four weeks with seventy-nine recoveries; nine died, a mortality of 10.22 per cent. Table 6 shows that of the infants who had lost less than 20 per cent. of their best weight, forty recovered and only one died. Only one breast fed infant died, then, who had lost less than 20 per cent. of its body weight. It so happens that this infant was the one previously noted who died of postoperative hemorrhage, and in whose family there was a history of bleeding.

The total mortality for the artificially fed cases shown in Table 6 is 32.6 per cent. Twenty-five of these children had lost at the time of operation less than 20 per cent. of their best weight; there were four deaths, a mortality of 16 per cent. Twenty-one had lost 20 per cent. and more of their best weight, with eleven deaths, a mortality of 52.38 per cent. The advantage of breast feeding is very evident when the corresponding divisions in this group and in the artificially fed group (Table 6) are compared.

On an average, the ninety-four breast fed infants who recovered remained in the hospital after operation for 14.7 days; while with the thirty-seven artificially fed babies the average was 23.78 days. A breast fed baby recovering without any complications is usually discharged as soon as the wound is healed and the sutures are removed. As breast milk is used exclusively in the postoperative feeding, some additional time is required to put the artificially fed babies on a suitable formula. Hence, the necessity for a longer stay in the hospital.

The prognosis is greatly influenced by the postoperative care in these cases. The postoperative management as practiced in the Babies' Hospital has been published by E. A. Morgan.⁴ The routine has varied only slightly since the publication of this paper. Breast milk is indispensable. At first, very small quantities of diluted breast milk are given, and increases in amount and strength are made very

4. Morgan, E. A.: *Am. J. Dis. Child.* **11**:245 (April) 1916.

gradually. As it is necessary to measure very accurately and increase very carefully the amount of food given, the baby is not allowed to nurse until a week after the operation. Gastric and intestinal disturbances are easily produced in these delicate infants. Their intestines through prolonged starvation are often unable to handle large quantities of food, even though that food be breast milk. The slightest tendency to vomiting and loose stools must be regarded with grave concern. We have found it advisable for the first few days after operation to pass the stomach tube immediately before each feeding. This aids in the expulsion of gas and mucus and adds to the comfort of the baby. In the event of vomiting, the quantity of food should be reduced temporarily, and an occasional gastric lavage should be given with 1 per cent. sodium bicarbonate solution. If the stool becomes loose, protein milk is used for a day or two instead of breast milk.

CONCLUSIONS

1. The duration of symptoms prior to operation is probably the most important single factor affecting the prognosis. When symptoms have lasted less than four weeks, the mortality is only one third as great as when they have lasted four weeks or longer.

2. The mortality in artificially fed babies is more than three times that for the breast fed babies.

3. In infants weighing 7 pounds or less, the mortality was three and one-half times as great as in those who weighed more than 7 pounds.

4. The mortality increases in direct proportion to the amount of weight lost previous to operation.

5. The mortality for breast fed infants who had vomited less than four weeks and who had lost less than 20 per cent. of their best weight is almost nil. The fatalities which occur are due to accidents usually avoidable when the operation is done by a skillful surgeon.

We wish to express thanks to Dr. L. Emmett Holt for his valued advice in the preparation of this report; and to Dr. Wm. A. Downes for the privilege of using his records.

STUDIES WITH A NEW METHOD FOR DETERMINING THE COAGULATION TIME OF THE BLOOD IN THE NEW-BORN *

F. C. RODDA, M.D.

Assistant Professor of Pediatrics, University of Minnesota

CHILDREN'S CLINIC OF MINNEAPOLIS

In pursuance of studies on the coagulation time of blood in the new-born clinic of the pediatric department, University of Minnesota, there was found a host of methods from which to choose, none of which were particularly adapted to the work or gave dependable results.

Since Vierordt's early studies on blood coagulation many ingenious devices and methods have been employed. Hinman and Sladen¹ gave a history and résumé of the work. The more practicable of these methods fall into certain types, and these were studied.

First, was considered Wright's² method and its many modifications. These, however, call for the use of special, carefully calibrated tubes with very close temperature control. Even so, results vary widely. Another type of method was introduced by Milian³ and modified by Duke, Hinman and Sladen.⁴ This method, however, gives marked variations according to the quantity of blood deposited on the slide, and Duke's⁴ technic requires a specially constructed slide, hard to obtain. Brodie and Russell's⁵ instruments, with modification by Boggs, present another scheme. These instruments, however, are special, expensive, require the use of a microscope and are not practicable for general bedside use. Besides, the method employs a current of air directed against the drop. Differences of humidity, temperature and force of the air current introduce factors which affect the results and are hard to control.

Howell criticized all methods employing blood obtained by skin puncture because of the mixture of tissue juices which shorten the

* Read before the Northwestern Pediatric Society.

1. Hinman, F., and Sladen, F. J.: Measurements of the Coagulation Time of the Blood and Its Application, *Johns Hopkins Hosp. Bull.* **18**:207, 1907.

2. Wright, A. E.: On a Method of Determining the Condition of Blood Coagulability for Clinical and Experimental Purposes, *Brit. M. J.* **2**:223, 1893.

3. Milian, G.: Le Causes d'erreur dans l'étude Clinique de la Coagulabilité du sang, *Presse méd.* **1**:202, 1904.

4. Duke, W. W.: A Simple Instrument for Determining the Coagulation Time of the Blood, *Arch. Int. Med.* **9**:258 (March) 1912.

5. Brodie, T. G., and Russell, A. E.: The Determination of the Coagulation Time of the Blood, *J. Physiol.* **21**:403, 1897.

time. His method, as modified by Lee and White,⁶ in which the blood is obtained by venipuncture and the clotting time obtained in a small glass tube, is the most often employed. Doubtless, it is the method which, when carefully followed, comes nearest to giving the absolute coagulation time. However, the venipuncture must be done skillfully, with minimal injury to the vessel wall, and the blood must be obtained without the admission of air bubbles, or widely varying results occur. Also, the end result is not sharply defined.

In work on the new-born one is at once confronted with the difficulty of obtaining blood from a superficial vein. It is extremely difficult, often impossible. It is true, one can enter the superior longitudinal sinus, but this requires a special technic. Even the most experienced often fail to enter the sinus because of distortion from molding of the head. It is especially difficult in the first days of life, and besides, the procedure of thrusting a needle through the scalp into the cranial cavity is not always innocuous. It surely is no routine to be practiced by a novice in the home.

A method was, therefore, sought which would require little special apparatus and be simple, easily applied in the home by any physician engaged in the care of the new-born. A return was made to the drop method. All factors such as depth and site of puncture, size and sequence of the drop, temperature, air currents, and the effect of foreign bodies in contact with the blood, were duly considered. An effort was made to control and standardize all these factors and still have the procedure simple and easy of application in the ward or the home. After many trials the following method was evolved.

METHOD

The apparatus required consists of a spring lance (a simple scalpel will suffice), two one and one-half inch watch glasses and No. 6 lead shot, all of which are easily obtained and transported. Glass and shot should be cleaned, preferably by washing with soap and water followed by alcohol and ether. Needless to state, the lance should be sterile, which implies freedom from old blood. The heel of the infant is sponged with ether, a puncture is made with the lance blade set (about 0.5 c.m.) to produce a free flow of blood without the slightest pressure. A clean watch glass containing a No. 6 shot receives the second drop of blood. A second watch glass is inverted over the first. The watch glasses are gently tilted every thirty seconds until the shot no longer rolls, but is fixed in the clot. The end-result is sharply defined, the shot is firmly embedded, so that the glass may be inverted without dislodgment of the shot. At times, due to the forcing out of

6. Lee, R. L., and White, P. D.: A Clinical Study of the Coagulation Time of Blood, *Am. J. M. Sc.* **145**:495, 1913.

serum, the whole clot may move, carrying the shot with it. This is no source of confusion, for the shot will be found enmeshed in the fibrin and there is no rolling or rotation of the shot. A poorly formed clot or one showing slight retraction is patent, for in such instances the shot continues to roll.

An effort was made to comprehend and check all sources of error. Coating the shot with paraffin did not affect the time. Watch glasses of the same size and curve were employed to standardize the surface area of the drop in contact with glass. The inverted watch glass minimizes the drying of the drop and prevents the entrance of lint and dust. All the work was done in the new-born ward, and the slight variations of the room temperature did not affect results. The greatest source of error is concerned with the blood flow. A small, slowly forming drop obtained by pressure clots very quickly, the tenth drop more quickly than the second. Depth and extent of the cut show no influence as long as the flow of blood is free and occurs without

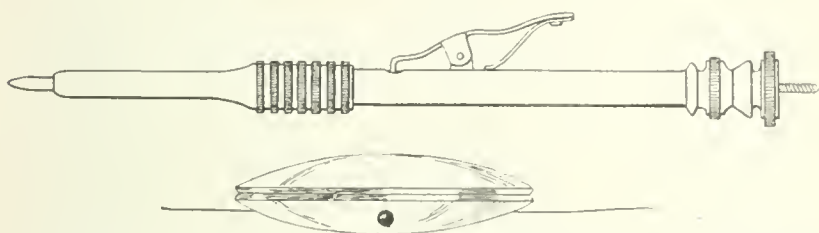


Fig. 1.—The apparatus used consists of a spring lance, two watch crystals and No. 6 lead shot.

pressure or squeezing. In all the determinations the blood flow was free. The first drop was discarded, the second drop, only, employed, and time was reckoned from the moment that the first drop fell. The time consumed in the formation of the second drop was considered a part of the coagulation time. Determinations were made to the nearest half minute.

No claim is made that the absolute clotting time is obtained, but the result is, at least, a clean cut relative time for comparative work. The object is to find gross variations from a normal range. The question is not whether the clot forms in six minutes or in six minutes and forty-five seconds, but whether it forms in six or sixteen minutes.

This method was checked with that of Lee and White in a series of thirty-eight determinations done on the same infants at the same time, blood being obtained for the Lee and White method from the superior longitudinal sinus. The average time was the same—seven minutes—for both methods. This was quite unexpected, for it has been assumed that all methods employing skin puncture give shorter

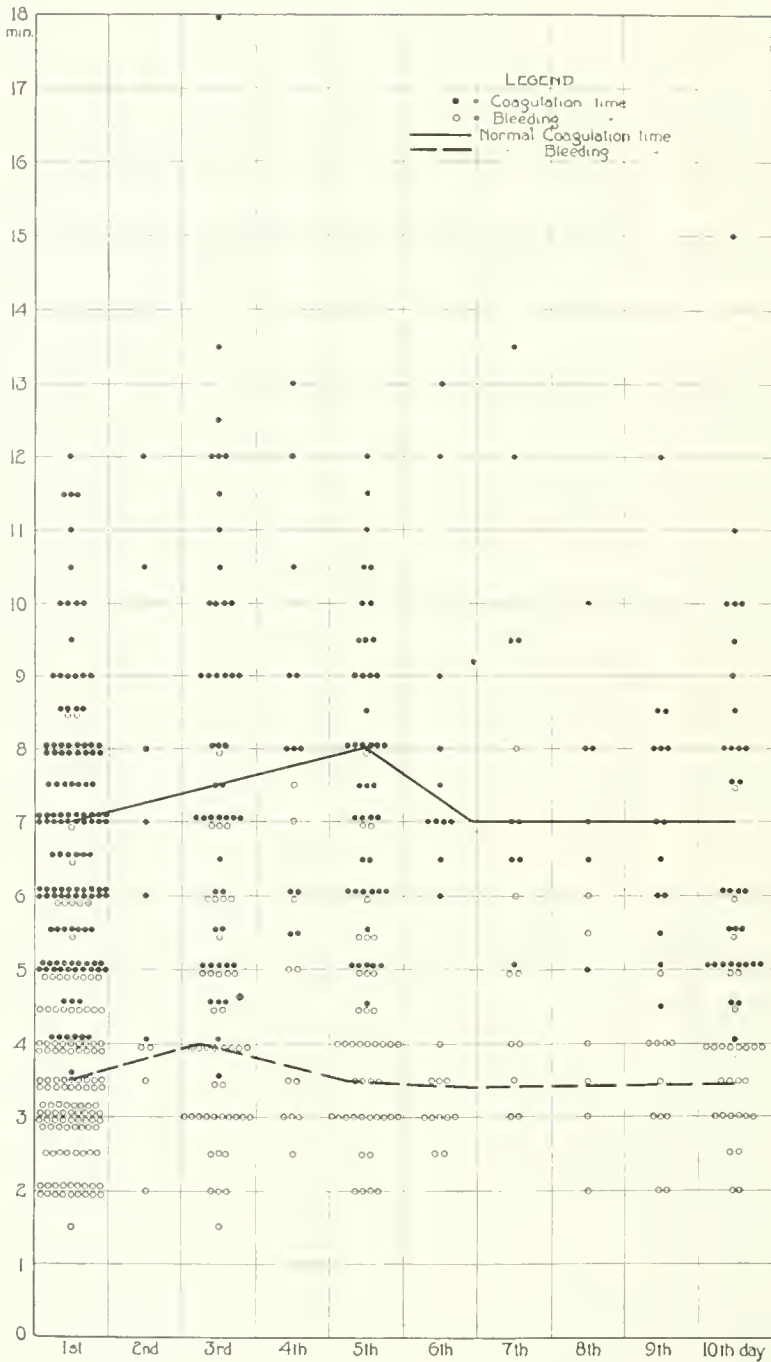


Fig. 2.—Determinations of coagulation and bleeding time on various days of first ten.



Fig. 3.—Coagulation time in a series of cases above the normal range.

clotting times. Further, the Lee and White method showed a greater variation than the drop method. In the series with the Lee and White method the arithmetical deviation from the average of seven minutes was two and one-half minutes, or 36 per cent., while the drop method gave a variation of one and one-half minutes from the average of seven minutes, or 20 per cent. In the same series the standard deviation with the Lee and White method was approximately three and one-half minutes, and with the drop method two minutes. In a small series of adults and older infants and children the results with the method coincided with those obtained in the new-born.

The average coagulation time determined on 126 new-borns within the first twenty-four hours of life was seven minutes with an arithmetical deviation of one and one-half minutes, giving an approximate range of from five and one-half to eight and one-half minutes, or roughly, from five to nine minutes. Eighty per cent. of all determinations fall within this range, while a range of from four to ten minutes included 95 per cent. of all the cases. It may, then, be stated that with this method the average coagulation time is seven minutes—that a time of more than ten minutes presents delayed coagulation.

It was early noted that the coagulation time varied on different days of the infant's life, showing a tendency to prolongation over the second, third and fourth days with a maximum on the fifth day, and a return to the time obtained during the first twenty-four hours before the tenth day.

Determinations with the method were then made on various days of the first ten, the majority being taken on the first, third, fifth and tenth days. A field graph and a median curve of the results were prepared. Because of the smaller number of determinations on the second, fourth and sixth days, combinations of second and third, fourth and fifth, sixth and seventh, eighth and ninth days were made. The result is then a weighted curve of the median. It is to be noted that the curve reaches the highest points on the fourth and fifth days. It is significant that this corresponds with the age incidence of hemorrhagic disease in the new-born.

The bleeding time, using Duke's ⁷ method, was also determined, and a similar weighted curve constructed. It shows the same general type of curve as that of the clotting time. The average time in the same 126 cases was three and one-half minutes, with an average deviation of one and one-half minutes, and a range from two to five minutes. A bleeding time of from two to five minutes may be considered normal for the new-born.

7. Duke, W. W.: The Relation of Blood Platelets to Hemorrhagic Disease, *J. A. M. A.* **55**:1185 (Oct. 1) 1910.

A study was then made of a series of cases presenting coagulation times above the normal range. In this chart the curves of the average normal coagulation and bleeding times are shown, also four abnormal ones with case numbers. It is to be noted, that all these cases presented an exaggeration of the normal curve of coagulation time. It is further to be noted that in two cases a prolonged bleeding time accompanied the delayed coagulation time. In Cases 2 and 3 hemorrhages appeared. In Case 2 a marked hematuria occurred on the fourth day. Blood was given subcutaneously, the reactions returned to normal and the hematuria cleared up. In Case 3 convulsions developed, and other signs of cerebral hemorrhage, on the second day. Blood was given subcutaneously; a decompression operation was performed on the fifth day. Recovery was complete.

On the other hand, cases showing prolonged coagulation time, accompanied by a normal bleeding time, showed no signs of hemorrhage (Cases 5 and 6). It would appear, therefore, that the hemorrhagic factor is a complex of delayed coagulation time and prolonged bleeding time. Further, variations from the normal range of coagulation and bleeding times are due to some deficiency of coagulation properties or excess of anticlotting substances which may gradually be overcome. This may be hastened by the subcutaneous administration of blood (Case 2). In all the cases a return to normal finding occurred by the tenth day. Further studies on calcium, prothrombin, "anti-thrombin," and fibrinogen content of the new-born blood are under way.

SUMMARY

1. The method is simple, easily applied in the new-born and gave results more accurate than those obtained with the Lee and White method.

2. The average coagulation time in the new-born with the method is seven minutes, with a normal range of from five to nine or ten minutes. The average bleeding time in the new-born with Duke's method is three and one-half minutes with a normal range of from two to five minutes.

3. In the normal new-born there is found a tendency to prolongation of these times in the first days of life. Hemorrhage is accompanied, in many cases at least, with an exaggeration of this tendency or markedly prolonged coagulation and bleeding times.

4. The coagulation and bleeding times should be studied in conjunction.

5. Routine determinations in the new-born will allow the selection of at least certain of the hemorrhagic conditions before the onset of symptoms and give the indication for the administration of blood.

6. The method will allow of a check on blood therapy in hemorrhages of the new-born.

7. Further studies may help to clarify the complex known as hemorrhagic disease of the new-born.

The writer is indebted to Prof. R. E. Scammon of the Department of Anatomy for valuable suggestions and help in preparing the field graphs and curves.

CLINICAL DEPARTMENT

ROENTGEN-RAY DEMONSTRATION OF ABNORMALITIES OF THE GASTRO-INTESTINAL TRACT IN CHILDREN *

CHARLES GILMORE KERLEY, M.D.

NEW YORK

We have thus far made roentgen ray studies of sixty-six cases of chronic gastric intestinal disorders in children from 3 months to 15 years of age. The vast majority were between 3 and 6 years of age. Many roentgenograms were taken, in some instances as many as twenty, in order to determine the emptying time of the stomach or intestine, or both.

CASE 1.—*Megacolon; dilated sigmoid.*—A boy aged 8 years, had an enormous sigmoid pouch with a capacity of at least two pints (Fig. 1). There was displacement of the liver due to the pressure exerted by the massive dilatation of the colon. The bismuth meal did not disappear entirely from the intestinal canal in seventeen days. One can readily appreciate what a difficult matter it would be to carry out any satisfactory treatment in a case of this kind without roentgen-ray examination. There was extreme abdominal distention and moderate malnutrition.

CASE 2.—*Acute pylorospasm.*—This patient was a boy, 7 years of age. The roentgenogram (Fig. 2) shows that the stomach is in active peristalsis, with a pronounced pylorospasm, three hours after the ingestion of the bismuth meal. The boy had been ill for one week with extreme paroxysmal pain in the stomach to such a degree that morphin had to be administered repeatedly. It will be observed that but little of the bismuth meal had passed through the pylorus three hours after the meal was given.

CASE 3.—*Constipation; elongated sigmoid.*—A boy, 6 years of age, came under observation because of obstinate constipation. There had never been an evacuation without assistance since birth. Drugs or local measures were resorted to daily. The roentgenogram (Fig. 3) of the intestine shows that the flexure of the sigmoid passes above the umbilicus and up to the transverse colon, and that the sigmoid is correspondingly elongated.

CASE 4.—*Diarrhea; triple sigmoid.*—This patient was a female, 20 months old, weighing 22¼ pounds. There was a triple sigmoid (Fig. 4). During the early months of her life she suffered from obstinate constipation and about two months before coming under treatment a diarrhea developed which had continued and which it was impossible to control. There was great abdominal distention, assimilation was very defective and death followed from exhaustion. It has been found that in cases of this type a chronic mucous colitis or diarrhea is very apt to follow prolonged constipation.

CASE 5.—*Recurrent vomiting; elongated sigmoid.*—This patient was a girl, aged 4 years. The stomach had not begun to empty in one and one-half hours after the bismuth meal, showing a decided pylorospasm (Figs. 5, 6 and 7). For two years the child had been a sufferer from seizures of recurrent vomiting, the

* Read before the American Pediatric Society, Atlantic City, June, 1919.

attacks lasting from two to four days. It was unusual for three months to pass without an attack. Figure 6 shows that there is retention in the stomach after five and one-half hours. Complete emptying requires about eight hours. Figure 7 shows that the child has an elongated and redundant sigmoid. There was habitual constipation and moderate abdominal distention.

CASE 6.—*Pylorospasm; angulated sigmoid.*—This was a case of marked pylorospasm. The child was a female, aged 3 years, weighing 17 pounds and 3 ounces. She had been subject to periodic vomiting attacks since birth, having a seizure about once every six weeks. There was marked malnutrition, which can readily be appreciated when one takes into consideration her age and weight. She had retention of food six hours after feeding (Fig. 8), which was corroborated by stomach tube examination. In addition to the malnutrition there was a pronounced secondary anemia. The abdominal distention was extreme. Figure 9 shows food residue in the stomach five hours and forty-eight minutes after a bismuth meal. Figure 10 represents the large intestine of the same child. There is a sharp angulation at the junction of the descending colon and sigmoid which probably accounts for the obstinate constipation and the abdominal distention. It was only through the use of enemas or drugs that an evacuation was produced. In angulations of this type it has been found that fecal matter will pass through the intestine more readily than gas.

CASE 7.—*Pylorospasm; wandering stomach; enlarged sigmoid.*—The patient, a female, 5 years of age, had pylorospasm, with the stomach displaced to the left, a so-called wandering stomach. There was a large gastric retention six hours after the bismuth meal (Fig. 11). The retention was repeatedly corroborated by stomach tube examination. The child suffered from habitually poor appetite and there was moderate malnutrition and habitual constipation. The abdomen was greatly distended. Figure 12 shows marked elongation of the sigmoid, extending two inches above the umbilicus and to the right as far as the intestine could pass.

We have found in these patients with elongated and sacculated sigmoids and resulting stasis that the emptying time of the stomach is always delayed. There seems to be direct association between the emptying time of the stomach and that of the large intestine. A peculiar feature of these cases of retention is loss of appetite. The patient will, perhaps, have a fair appetite for breakfast when the stomach is empty. The other meals must be forced or coaxed into the child.

CASE 8.—*Gastroptosis; poor appetite; malnutrition.*—The patient was a female, 16 years of age. There was marked ptosis of the stomach (Fig. 13) and an extreme prolapse of the transverse colon (Fig. 14). This patient was anemic, undersized and underweight. The only active symptom was a persistent pain in the left lower abdominal quadrant. There was no symptom referable to the stomach other than poor appetite and eructation of gas. There was moderate abdominal distention. Medication was required daily to produce an evacuation.

CASE 9.—*Gastroptosis; recurrent vomiting; malnutrition.*—This patient was a male, 11 years of age. The lower portion of the stomach is ptosed $2\frac{1}{2}$ inches below the umbilicus (Fig. 15). The colon is also ptosed to such a degree that with a full bladder, the bladder, stomach and colon would come in close contact (Fig. 16). This boy suffered from periodic vomiting and had been treated for acidosis for several years. There was moderate abdominal distention and habitual constipation. The bowel function required daily supervision.

We have learned a great deal through our roentgen-ray studies. First, we have learned that there may be persistent gastrointestinal derangements affecting the immediate and after-life of the



Figure 1



Figure 2



Figure 3



Figure 4



Figure 5

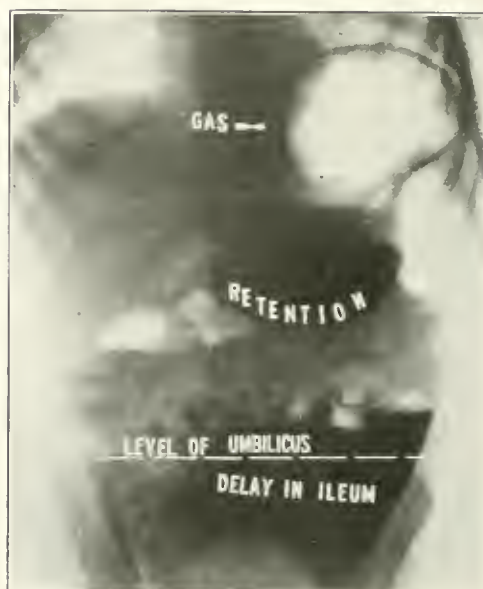


Figure 6

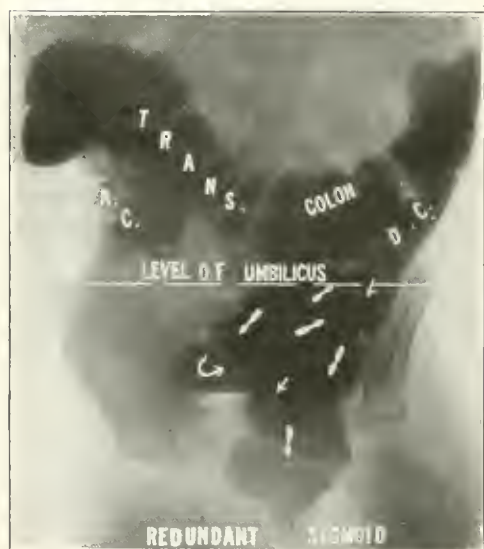


Figure 7



Figure 8

patient, dependent entirely on mechanical agencies. The gastrointestinal tract of the runabout child has been given the credit of being *structurally* normal, and physicians have relied on examination of the gastric contents, stools and urine with the idea of finding the causes of gastro-intestinal derangements. Our roentgen-ray studies have demonstrated that periodic or so-called recurrent vomiting, which repeatedly had been diagnosed as a manifestation of acidosis, is due, in many instances, to a dilated or ptosed stomach in which there is retention and residue long after the feeding period. Fresh food is given to these children at fairly regular intervals, in a stomach that is never empty, except in the early morning. Nature comes to the relief of the case after a time, and the stomach is emptied periodically at fairly definite intervals.

Another feature of importance relates to the appetite. We have found repeatedly that children who will not eat willingly, and who have to be coaxed and forced, may have a stomach of defective emptying capacity. A child will not be hungry in the event of food remaining in the stomach, beyond the next regular feeding period. It is our effort in these retention cases to leave a long interval between the feedings. Breakfast at 7:30 a. m., dinner at 12:30 or 1 p. m., and supper at 6 p. m. Water only is allowed between meals. With such intervals and measures employed to insure a free daily bowel evacuation, it is surprising how soon many children will develop a normal appetite.

The stomach of the normal child is emptied in from four to four and one-half hours after a meal. Food residue found five hours after a meal means a stomach of slow emptying capacity. We have further proved that there is unquestionably a relation between the emptying time of the intestine and that of the stomach. When intestinal stasis is relieved in a residue case, the stomach empties normally.

In Case 8 there was gastropsis with surprisingly few active symptoms, other than pain, constipation and capricious appetite. Patients of this type show other symptoms, however, which are of interest. They are always undernourished. They are anemic and irritable in disposition and show faulty growth. They are ill, but the fact is not appreciated because they are as well as usual. They are the type which later in life furnishes work for the abdominal surgeon.

With the view to checking up our observations roentgen-ray studies have been made of children who were not ill. It has been rare to find a dilated or ptosed stomach that did not give rise to symptoms, symptoms which in some instances had not been appreciated. A ptosed colon gives trouble. Not all elongated sigmoids, however, produce symptoms. There may not even be constipation, provided there are no sacculations, adhesions or relaxed abdominal muscles.



Figure 9



Figure 10

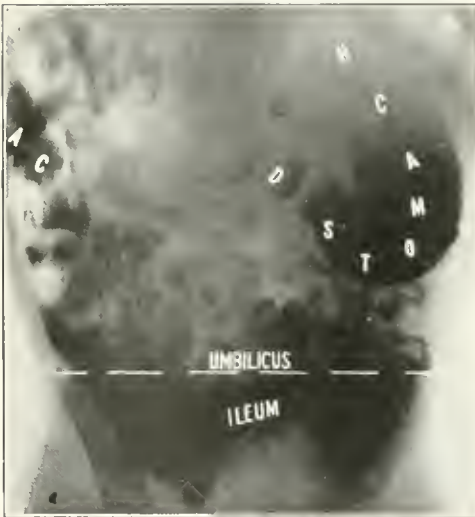


Figure 11

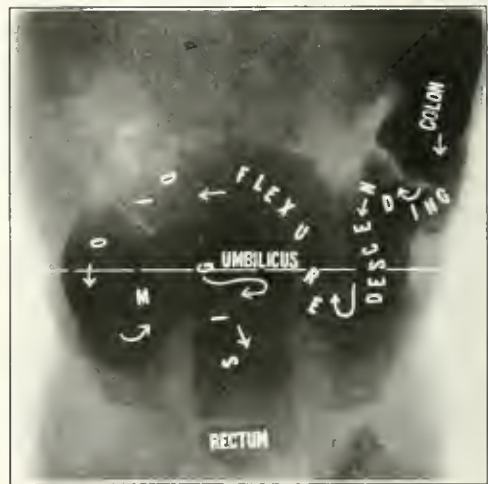


Figure 12



Figure 13

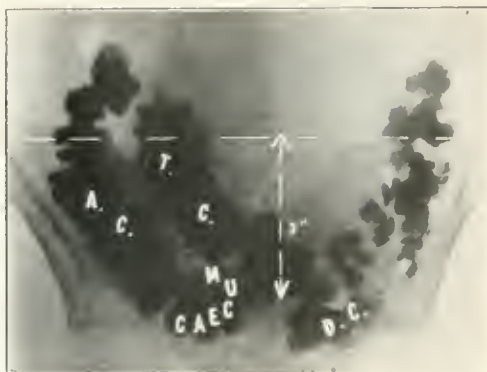


Figure 14



Figure 15



Figure 16

Given a relaxed abdominal wall, a generally distended abdomen and an elongated sigmoid, we have a condition fertile in possibilities for gastro-intestinal disturbances. Weak, relaxed abdominal muscles play an important rôle in these cases. When we supply adequate support, such as a tight-fitting abdominal belt, the relief furnished is very striking. The query has perhaps arisen as to what constitutes a normal sigmoid. I believe that Figure 17 represents such a case. The child was 5 years old. Figure 18 represents a normal sigmoid in a child 8 years of age.

Management.—Only general suggestions as to treatment can be made. Probably the most useful individual measure that applies to



Figure 17

all types of abnormalities, both of the stomach and intestine, is in the use of a well adjusted abdominal belt. For those cases in which the stomach alone is ptosed, a belt with a projecting narrow pad, a so-called shelf, is employed. The device is placed on the belt in such a position as to support the displaced stomach. In those cases in which the intestine alone is involved and in those cases in which there is a gastropotosis, an abdominal belt with a large flat pad is used. The belt is worn constantly when the patient is up and about.

Diet.—In cases of ptosed stomachs in which there is always a delayed emptying, three meals daily only are allowed, and these meals are given at as long an interval as possible. It has been found advisable to give but little fluid with the meals. After each meal, the patient rests in a recumbent position for one hour.

Massage.—In the cases of intestinal stasis, abdominal massage is practiced daily. It has been demonstrated that this measure is of much benefit.

Drugs.—Peristalsis has been shown to be defective when gross intestinal abnormalities exist. In addition to massage for the re-establishing of this function, certain drugs are of value. Small, frequently repeated doses of a combination of nux vomica, belladonna and cascara have been of much aid in producing a more active peristalsis and thus helping to relieve the ever present constipation. But whatever medication is selected, it should be given not less than three times a day. In cases of sacculation and dilatation of the intestine, a full dose of



Figure 18

liquid petrolatum is given once a day. Enemas are to be used only as an emergency measure. Atropin is given in full doses when there is an evident pylorospasm.

The roentgen-ray studies on which these observations were made were carried out by Dr. L. T. LeWald, director of the roentgen ray department at St. Luke's Hospital.

The patient is prepared the evening before by taking a cathartic and the next morning, before the injection, a cleansing soap sud-enema is given. A light breakfast is allowed if desired. The opaque substance—barium sulphate—chemically prepared for roentgen-ray purposes, is mixed with fermented milk in the proportion of one part of opaque substance to six parts of the suspending medium. A sufficient quantity is used to fill the colon. This varies with the age of the

patient and the size of the colon, as previously determined by roentgen-ray examination by means of the opaque meal.

The opaque meal is made up of one part of bismuth subcarbonate suspended in eight parts of the ordinary feeding mixture in infants, and for older children it is suspended in fermented milk. If the infant is unable to take the food the ordinary way, it is fed by means of a tube attached to a funnel.

PROGRESS IN PEDIATRICS

RÉSUMÉ OF LITERATURE ON TUBERCULOSIS IN CHILDREN DURING 1918 AND 1919

MAY MICHAEL, M.D.

CHICAGO

MODE OF INFECTION

J. O. Cobb¹ is of the opinion that tuberculous infection in man and animals is generally brought about by the ingestion method. He believes that even where the bacillus is planted on the respiratory mucous membrane by means of dried sputum or by dried feces, as often happens with cattle, the anatomic method is still through the intestinal tract, because the number of bacilli that would be swallowed is out of proportion to the very doubtful number that might possibly reach the air vesicles by inhalation. Cobb agrees with Aufrecht that tubercle bacilli gain entrance into the circulation, however introduced, and then traverse the blood vessels as foreign bodies, until arrested in some organ, most commonly in the pulmonary terminal arteries. Here the bacillus passes through the thin vessel wall barrier, to be picked up by lymphocytes and promptly carried to the nearest lymph gland. Moreover, all portions of the lungs, in man and in animals, are invaded by dust and tubercle bacilli in equal measure, whether the route be through the trachea or through the intestinal tract.

F. Clark² says that the importance of tuberculosis can hardly be overestimated, when it is realized that one-fourth of all children give evidence of tuberculous infection. He shows that the route of infection is still of great interest to investigators, and that the majority of pathologists believe that there is always present a primary focus in the lungs. Investigators have also been interested in establishing the fact that tuberculosis in the adult is simply a lighting up of the process which started in childhood. E. L. Opie, however, has shown by a series of necropsies that apical tuberculosis in adults has no relation to the focal tuberculosis occurring in children, nor is it caused by it. Clarke believes that there is not enough evidence for the conclusion that all cases of tuberculosis in adults have their origin in childhood.

Since the publication in 1912 of A. Ghon's work on tuberculosis in childhood, his ideas as to the primary focus in the lung with secondary lesions in the bronchial glands have been generally accepted, as also has been the fact that infection in the adult is only a lighting up

1. Cobb, J. O.: The Point of Election and Modes of Invasion in Pulmonary Tuberculosis, *J. A. M. A.* **70**:1511 (May 25) 1918.

2. Clarke, F.: Tuberculosis in Children, *Nebraska M. J.* **3**:158 (Feb.) 1918.

of an old infection of infancy or childhood. Lately, however, the opinion is gaining ground that apical tuberculosis in adults does not depend on an infection of childhood, but is a secondary infection. The work of Opie, quoted by Clark, and abstracted in the résumé of 1917, is strong evidence in favor of this later view.

C. Chomé³ adds the report of another case of congenital tuberculosis to the few found in medical literature. The child's mother died of tuberculosis twenty-four hours after his birth. On the seventh day the baby developed a cough and an irregular temperature. Auscultation revealed many râles. The child gained weight so slowly that when 2 months old he had not recovered his birth weight, although no digestive disturbance was apparent. The child was always pale, but had red lips. During the second month, tubercle bacilli were obtained from the stools. The endodermal tuberculin reaction was negative. The child died when 3 months old. Necropsy disclosed tubercles scattered through both lungs. The hilus glands were very large and caseated. The spleen showed miliary tubercles. In the tympanic cavities was fluid, from which tubercle bacilli were isolated. Evidently the case was one of congenital tuberculosis. There could hardly be a possibility of infection during delivery, as the child was delivered a few minutes after the bag of waters ruptured. The mother never saw the baby, so that infection later was impossible. The appearance and predominance of the lesions in the bronchial glands leads the author to believe that here the bacilli were first arrested.

BACTERIOLOGY

From her study of the literature, Mildred C. Clough⁴ concludes that in all forms of tuberculosis, except the miliary form, the occurrence of tubercle bacilli in the circulating blood in quantities large enough to infect a guinea-pig is relatively infrequent, while in miliary tuberculosis sufficient numbers occur in a large percentage (66.6 per cent.) of the cases. Clough's study reveals only one case in which tubercle bacilli have been cultivated directly from the blood of tuberculous patients. She has, however, been able to grow tubercle bacilli in cultures from the blood of five patients (four of them children) suffering from miliary tuberculosis. In the first three cases she used a medium of 5 per cent. glycerin broth, made neutral or slightly acid. After a preliminary incubation the contents of the flasks were centrifuged and the sediment planted on blood agar slants. In the next two cases the blood was hemolyzed with distilled water and cen-

3. Chomé, E.: Case of Congenital Tuberculosis, *Arch. mens. d'obst. et de gynec.* 7:294 (Oct.-Dec.) 1919

4. Clough, M. C.: Cultivation of Tubercle Bacilli from the Circulating Blood in Miliary Tuberculosis, *Am. Rev. Tuberc.* 1:598 (Dec.) 1917; also *Bull. Johns Hopkins Hosp.* 28:363 (Dec.) 1917.

trifuged, and the sediment planted directly on blood agar slants. Clough suggests the use of this method as an aid in the diagnosis of acute miliary tuberculosis, since results are obtained much more quickly than by guinea-pig inoculation.

R. S. Austin⁵ analyzed twenty-four cases of tuberculosis in children and infants with special reference to the type of infecting organism. He also made an attempt with each patient coming to necropsy to ascertain the primary focus of infection, basing his conclusions on the lesion which appeared to be the oldest.

Determination of the human or bovine type of bacillus in each case was made by inoculation of rabbits with known amounts of cultures. Each rabbit received also a corneal scratch, into which was rubbed a drop of the bacillus suspension used for inoculating the animal. The other cornea was similarly scratched and rubbed simply with saline solution as a control. The corneal scratch test, however, was not very satisfactory. Although consistently negative in rabbits with the human type of infection, it was not always positive in animals with the bovine type of infection.

Austin found that seven of the twenty-four patients were infected with the bovine type of tubercle bacillus. The primary focus was found in twelve cases. In six cases it was situated in the right lung, in two in the left lung, in three in a bronchial lymph node on the right side, and in the intestine in one case. Although this is too limited a series to permit of drawing definite conclusions concerning the incidence of bovine tuberculosis among children, Austin believes, nevertheless, that the finding of the bovine type of organism in seven out of twenty-four cases emphasizes the etiologic importance of this variety of tubercle bacillus in tuberculosis in children.

R. S. Austin⁶ examined for tubercle bacilli the tonsils excised from forty-five children, who clinically showed no evidence of tuberculosis. He made inoculation tests on guinea-pigs, histologic examinations of sections, cultures on Dorset egg medium, and direct smears from the tonsils. In none of the cases did histologic examination, direct smears or cultures show tubercle bacilli. In one instance, a child aged 4 years, the inoculation test yielded the human type of organism. The child's parents were living and well, and there was nothing to point to tuberculosis in the past history of the child. These results tend to confirm the opinion held by many investigators that the surest test for the presence of tubercle bacilli in tissues or other pathologic material is the inoculation test. Austin thinks it of interest that in his one positive

5. Austin, R. S.: Bovine Tuberculosis in Children, *Am. J. Dis. Child.* **17**: 264 (April) 1919.

6. Austin, R. S.: Bacillus of Tuberculosis in Tonsils of Children Clinically Nontuberculous, *Am. J. Dis. Child.* **18**:14 (July) 1919.

case the organism should have been the human type of bacillus, and calls attention to the fact that in the few reports on the types of the tubercle bacillus found in the tonsils of children the bovine type predominates. The children in Austin's series, however, came from a community where the supply of cow's milk was not likely to be contaminated with the tubercle bacillus. The author finds that, although tuberculosis of the tonsils in children is not rare, yet, it occurs most often when there are other tuberculous lesions in the body, especially in the cervical lymph glands. The occurrence, however, of the tubercle bacillus in the tonsils of children without clinical evidence of tuberculosis, is not frequent.

SYMPTOMATOLOGY

J. Ritter⁷ discusses the course of tuberculous disease at different ages. He says that in infancy and early childhood, if the infection is a massive one, no organ or tissue is spared, and the child dies from a generalized tuberculosis and rarely sees the middle of the second year. Infants, mildly infected during the first year, as well as all children infected during the second and third year, who are either massively or mildly infected, form the great army of children who in the following years are victims of some form of tuberculosis, usually tuberculosis of the tissues and organs supplied by the greater circulation, rather than tuberculosis of the lung. In infancy and early childhood the glands about the hilus and near the bronchial bifurcation, the epibronchial, peribronchial, tracheobronchial, bronchopulmonary and even the tracheal glands are enlarged. These glands usually check the inroads of the virus, and the tuberculous process remains quiescent. Between the ages of 5 and 14 years there is an especial tendency to bone involvement. Up to the sixth and seventh year, the small bones and joints are chiefly affected, but, as the child advances toward puberty, the larger joints, the knee, ankle, shoulder and hip joints are most frequently the seat of tuberculous disease. After the fourteenth year the lungs, which have been more or less spared, are attacked.

The mortality from tuberculosis in early life is 98 per cent. or more; 50 per cent. at the age of 3 years; 20 per cent. at the age of 7, and at puberty only about 2 per cent. After puberty the mortality rate ought to be zero, but at this period many insidious intercurrent conditions arise, which account for the acute, subacute and chronic forms of pulmonary tuberculosis so frequently seen after the fourteenth year. It is interesting to note that the ratio between tuberculosis mortality and infection is in inverse proportion. In early infancy, the infection is usually estimated at between 1 and 2 per cent., with a

7. Ritter, J.: *The Course of Tuberculous Disease at Different Ages*, Illinois M. J. **32**:416 (Feb.) 1917.

mortality of nearly 100 per cent.; while at the age of 14 years the percentage of those who are infected reaches more than 95, with a mortality of only 2 per cent.

J. P. C. Griffith⁸ describes the following types of tuberculosis in childhood:

1. *General Tuberculosis*.—Two clinical forms of this type are seen. (a) The typhoid form: This is sometimes called acute miliary tuberculosis. It is observed chiefly in infancy and in early childhood. The initial symptoms are very vague. There is loss of appetite and weight and general impairment of health, combined with an irregular and entirely uncharacteristic fever. The symptoms strongly suggest typhoid fever, and it is only later, when the time for improvement in typhoid fever should come, that evidences develop of a pneumonia or more often of a meningitis, and the diagnosis of the typhoid form of acute miliary tuberculosis becomes evident. (b) The marantic form: This is observed not infrequently in infancy. The symptoms consist of progressive wasting and anemia. There is no fever, or at most occasional elevation of temperature, and no respiratory or gastro-intestinal disturbances to account for the condition. The symptoms can in no way be distinguished from infantile atrophy due to other causes, and the child finally dies of exhaustion. The diagnosis is made only at the necropsy. Sometimes a few weeks before the end of life evidences of bronchopneumonia develop or other localizing symptoms appear.

2. *Tuberculosis of Special Regions*.—(A) Tuberculosis of the lungs: There are several subdivisions. (a) Acute miliary tuberculosis of the lungs: This is only a form of the general miliary tuberculosis described, in which the localization in the lungs is from the onset the prominent symptom. It is most common about the age of 5 years. There is persistent fever, rapid respiration, prostration, rapid pulse, some cough and sometimes cyanosis. The physical signs are poorly marked. Later, the evidences of tuberculosis elsewhere may show, the child dying possibly from meningitis. At necropsy the lungs are found filled with miliary tubercles.

(b) Acute tuberculous bronchopneumonia: This is a very frequent form of tuberculosis, especially in infancy and early childhood. It may be primary in the lungs, or secondary to tuberculous lesions elsewhere. When bronchopneumonia occurs after measles or pertussis, there is always the likelihood that it may be tuberculous in nature; or when it comes after a period of wasting and ill health. Suggestive, too, is the prolongation of the attack after the time when a simple bronchopneumonia might be expected to resolve.

8. Griffith, J. P. C. Tuberculosis in Children. New York M. J. **109**:485 (March 22) 1919.

(c) Chronic pulmonary tuberculosis: This is the condition which in adult life is called phthisis. It is rarely found in infancy and early childhood and even in later childhood it is uncommon. Another form of chronic tuberculosis of the lungs is subacute or chronic tuberculous bronchopneumonia. This condition is more prevalent. A child may exhibit only moderate, occasional fever, progressive deterioration in health and other vague symptoms, and live for five or six months, only gradually exhibiting the physical signs of bronchopneumonia. Still another form is hilus tuberculosis, in which, in combination with the lesions in the lymph glands, there is a spread of foci of tuberculosis at the hilus of the lungs and along the course of the bronchial tubes. This may develop at any time in early life, even in infancy. The onset is insidious and the symptoms are vague, consisting principally of progressing malaise and debility, with occasional evening rises of temperature and a positive tuberculin reaction. Roentgenographic examination shows involvement of the tissues at the hilus, but does not differentiate the involvement of the lung from that of the bronchial glands.

B. Tuberculosis of the lymph glands: First to be noted in this connection is that of the bronchial lymphatic glands. This is very common, but does not present any positive characteristics. There is usually some loss of health, with more or less fever without discoverable cause. Roentgenographic examination may show decided thickening of the tissues about the hilus of the lungs, caused by disease of the bronchial glands here, the application of d'Espine's sign—the altered voice sound in the neighborhood of the seventh cervical and first dorsal vertebrae—is sometimes useful but cannot be depended on as being absolutely diagnostic. Tuberculosis of the mesenteric glands is a common localization, although less so than localization in the bronchial glands. As a rule, there are no clinically characteristic manifestations. Tuberculous cervical adenitis is by far the most frequent manifestation of tuberculosis in the external glands. It is especially common in early and later childhood. It may be accompanied by other evidences of tuberculosis, but usually is not.

C. Tuberculosis of the alimentary tract: The most frequent form of this variety of tuberculosis is that which is located in the intestine, producing the symptoms of ileocolitis. The diagnosis from other forms of ileocolitis depends chiefly on the discovery of the tubercle bacilli in the stools, or the presence of tuberculosis elsewhere in the body.

D. Tuberculosis of the genito-urinary tract: This is not a frequent manifestation in childhood. Tuberculosis of the testis is seen occasionally, but more rarely than of the female genitals. The kidney is involved in general tuberculosis, and less often the renal structure and the bladder may suffer from a more chronic form of the disease.

E. Tuberculosis of the nervous system: Apart from involvement of the meninges, the nervous system is not often attacked. Large solitary tubercles are sometimes found in the brain and spinal cord, and may give rise to localizing symptoms, but this is uncommon.

F. Tuberculosis of serous membranes: This may occur as one of the manifestations of general tuberculosis or it may predominate in, or be confined to, certain of the serous membranes, especially the meninges, the peritoneum and the pleura.

L. Ribadeau-Dumas⁹ describes in detail tuberculosis in infancy. He agrees with most writers that only exceptionally is the disease hereditary. He believes that it is contracted in infancy and its frequency increases with age. The highest points in the mortality curve occur at 8 months and 2 years; but the disease in infancy must not be regarded as always resulting in a general fatal tuberculosis, as was formerly taught. Early pulmonary manifestations do not occur, and failure of general health may be the first sign. The history of contact and result of tuberculin tests are, therefore, very important in infancy. Emaciation is a significant clinical sign, and any infant who fails to gain weight on a suitable diet must be studied carefully for tuberculosis or syphilis. The temperature curve shows, instead of the usual monothermia, a morning or evening rise. A valuable sign after the disease is localized in the bronchial glands is a dry metallic cough, spasmodic, like whooping cough. Sometimes, there is expiratory dyspnea from pressure of the enlarged glands. Auscultation reveals bronchial breathing as low as the fourth or fifth dorsal vertebra. Percussion over the manubrium in front and in the interscapular space behind gives an increased resistance. Pulmonary lesions give few physical signs, and often signs due to enlarged bronchial glands are wrongly interpreted as due to a pulmonary lesion. However, a localized area of râles which is persistent always gives rise to a suspicion of a pulmonary involvement. The author thinks that, on the whole, physical examination of infants is not very satisfactory, but that the roentgen ray can add much valuable information. Frequently, the presence of a surgical tuberculosis or of chronic miliary localization of the disease allows of the correct interpretation of the cachexia, emaciation and anemia. Cutaneous tuberculids, tuberculous gummata and phlyctenular conjunctivitis are manifestations of miliary localization and important aids in diagnosis.

The most frequent form of pulmonary tuberculosis in infancy is the caseous bronchopneumonic form. It shows nothing characteristic, except the failure to resolve and persistence of the physical signs. In

9. Ribadeau-Dumas, L.: Tuberculosis in Children, *Progrès méd.* **34**:312 (Aug. 9) 1919.

tuberculous pneumonia of infancy there is a marked tendency of the pneumonic areas to break down and form cavities.

Miliary tuberculosis in infancy runs a varied course. As a rule, the greatest number of tubercles are in the lungs and the picture is one of a capillary bronchitis. The roentgenogram is of great help and shows small disseminated irregular shadows, which clear up the diagnosis.

The prognosis of tuberculosis in infancy is grave. Among the author's cases the mortality was from 80 to 85 per cent. The severity of the infection seems to depend on the intensity of inoculation. A massive infection means a rapid course. There is considerable difference of opinion as to whether the cutaneous reaction is a guide to prognosis. Dumas quotes Jeanneret, who believes that tuberculous infants, without marked lesions, react feebly to tuberculin and have a tendency to become immune after repeated injections. Infants with pulmonary lesions are hypersensitive and give a reaction from 30 to 50 mm. in diameter; infants with tuberculous bronchial glands give an average reaction of 14 mm. in diameter. Infants with osseous tuberculosis give a very marked reaction, which remains stationary or diminishes in favorable cases, but increases in unfavorable cases. Infants with meningitis or miliary tuberculosis, at first give a very strong reaction, which becomes more and more feeble as death approaches.

Prophylaxis plays the most important rôle in the treatment of tuberculosis in infancy, and the writer lays great stress on the removal of the child from the tuberculous environment. He thinks the tuberculin, given intracutaneously, as advised by Jeanneret, offers hope in the treatment.

R. Raimondi¹⁰ gives the following symptoms of miliary tuberculosis, which he says often follows an attack of influenza. The infants are very pale and emaciated; early in the disease the appetite is diminished, but later anorexia is very marked. The stools are at first normal, and it is only after the intestines are affected that diarrhea supervenes. Sleep is little disturbed, but the infants cry out during sleep, as if in pain. The inguinal, axillary and submaxillary glands are enlarged. Cough is not a prominent symptom, unless the tracheo-bronchial glands are much involved. Percussion of the apices, sub-clavicular regions and infraspinous fossae does not give dulness but a relative resistance. Dulness may be obtained in the region of the hilus. Auscultation of these regions gives an exaggerated puerile respiration. Slight temperature persists through the entire course of the disease, which is from three weeks to three months. The prognosis is always fatal, some of the patients die with meningeal symptoms, some with intestinal symptoms.

10. Raimondi, R.: Tuberculosis in Infants, *Presse méd.* **26**:593, 1918.

From a careful comparison of a large group of tuberculous and nontuberculous school children, Priestley and Richardson¹¹ conclude that the weight and height ratio give little or no help in the diagnosis of tuberculosis in children, and that a previous attack of any of the common infectious diseases does not seem to predispose to attacks of tuberculosis. No evidence was found that tuberculosis is more common among those in poor environments than among those in good environment. The figures did not show that enlarged tonsils and adenoids, or caries of the teeth, or heart affections favor the development of tuberculosis. Enlarged cervical glands were much more frequent in tuberculous children than in nontuberculous children, and there were more cases of mental deficiency among them. There were also more instances of eye and ear disease, of anemia and malnutrition in the tuberculous group.

The authors describe the clinical picture of tuberculosis in children attending school. They found 283 cases of tuberculosis of all kinds; in eighty-seven instances the lungs were the seat of the disease. The evidence of pulmonary disorder which was noted in these were: Flattening and retraction of portions of the chest; dilation of the superficial veins; fibrillary contraction of the chest muscles; diminished expansion of part or whole of one or both lungs; diminished movement and increased vocal fremitus; alteration of the normal resonance, from slight impairment to absolute or wooden dullness; diminished respiratory murmur, cogwheel type of breathing, harsh or tubular breathing and adventitious sounds. Not in every case were all or even a great number of these signs present. In some there was little beyond poor expansion, slight dullness, cogwheel breathing and a few crepitations. Cough was present in the majority of the cases, sometimes the short, hacking, dry, spasmodic cough at night, suggesting pressure of enlarged bronchial glands on the recurrent laryngeal nerve. Hemoptysis, pain in the chest, anemia, loss of appetite and loss of weight were also noted.

Among the 283 cases of tuberculosis were 134 cases of glandular disease, involving the cervical glands in all cases, and the axillary glands as well in two cases. Tuberculosis of the glands was found in all degrees of development and severity. In forty-three of the 134 cases abscesses had ruptured spontaneously, leaving typical, bright red scars.

Tuberculosis of the bones and joints occurred in such a great variety of forms and affected so many parts of the body that a composite clinical picture was impossible. The tuberculous process usually affected a single joint or bone, was rarely seen in its active stage, but

11. Priestley, J., and Richardson, B.: Tuberculosis as Seen in Public Elementary Schools, *Brit. J. Child. Dis.* **15**:183, 1918.

chiefly when quiescent—so that the patients showed the results of the previous disease in deformities of varying degree, atrophy of muscles, marks of old sinuses and ankylosis or stiffness of joints.

Mary H. Williams¹² emphasized two signs in hilus tuberculosis. She says that over the lower part of the chest there is a flattening first on one side, then on the other. Over this area there is also a change in percussion note, which can better be felt than it can be heard. It can also be elicited by direct tapping with the finger tips. The second sign is a bilateral subclavicular flattening and is caused by the downward and backward pull of the fibrous bands connecting the healthy upper lobes with the healing and contracting areas at the base.

From his experience as a pathologist, E. Fisher believes that if chronic hilus tuberculosis does occur in children, it must be very rare. He is of the opinion that chronic disease of the lung in children is almost always nontuberculous, and makes the statement that, if a child acquires a tuberculous infection of the lungs, he is not likely to live more months than he has already lived years. Occasionally, a tuberculous infection may be grafted on a chronic nontuberculous disease. Primary tuberculous infection usually runs an acute or subacute course and very rarely is there found at necropsy evidence of fibrosis.

E. Fisher's statement in regard to the frequency of hilus tuberculosis and its prognosis is not in accord with the observations made by most clinicians. Bronchial gland tuberculosis with hilus involvement is a frequent form of tuberculosis in childhood and very often ends in recovery.

A Krause¹⁴ reports a case of healed multiple tuberculosis in a 14-year-old boy. When 4 years old he developed an osseous tuberculosis following a trauma. This was followed within a year by painless swelling of the epitrochlear and inguinal glands, and by abdominal distention. The lungs were normal at this time. The boy was given tuberculin treatment. The initial dose was 0.00001 mg., and this was increased to 1 mg. The sinus gradually healed and the glands reduced in size. Three years after the onset, however, the child was found to have impaired resonance over the right lung, and enlarged glands could be palpatated in the abdomen. At this time, he was still receiving tuberculin, 0.001 mg. at intervals of two weeks. The next year he developed an axillary abscess, which necessitated extensive dissection of the axillary glands. At the same time, there was a tuberculous

12. Williams, Mary: Hilus Tuberculosis in Children and Adults, *Lancet* **1**:682 (May 3) 1919.

13. Fisher, E.: Hilus Tuberculosis in Children and Adults, *Lancet* **1**:814 (June 1) 1919.

14. Krause, A.: Case of Multiple Tuberculosis in Childhood, *M. Clinics N. America* **2**:1781 (May) 1919.

peritonitis. The patient was then sent to a sanitarium, where he remained seven months. Since then he has not had any recurrence of active tuberculosis.

In discussing the case, Krause emphasizes the element of trauma as often being the exciting cause of an active tuberculosis. He thinks that in this case the primary infection was in the alimentary tract and involved the mesenteric lymph nodes, and from there it spread to other parts of the body. The tuberculin treatment was of little value, but the author believes that the reason for this was that the various foci of tuberculosis were in different stages of development, and it was impossible so to regulate the dosage of tuberculin that all foci would be acted on favorably. The sanitarium treatment was much more satisfactory. The discipline, the regularity of rest, exercise and diet, the life in the open, and the relief from strain, all were factors in producing the cure.

D. B. Leitch¹⁵ reports a case of tuberculous meningitis with xanthochromia and complete coagulation of the spinal fluid in a child 9 months old. Fourteen days before admission, the child had had a little fever and was more restless than usual. Four days later his head was retracted and he was so drowsy that he had to be aroused for his feedings. On admission to the hospital, the patient presented the typical picture of a tuberculous meningitis. A spinal puncture was made, and 15 c.c of fluid were removed. The fluid was slightly turbid and of a light amber color, resembling urine. The cells numbered 250 per c.mm., of which 76 per cent. were lymphocytes. Within ten minutes after withdrawal, the fluid coagulated to a jelly-like mass, so thick that the tube could be inverted without its contents spilling. The patient died on the third day, and postmortem examination showed the typical lesions of a tuberculous meningitis. There was a marked thickening of the membranes in the cervical region of the cord, and the author thinks the adhesions were quite sufficient to cause the obliteration of the sub-arachnoid space at this level. The spinal fluid in the lower portion of the canal was thus shut off from communication with the fluid in the ventricles, and it is in such conditions that the spinal fluid becomes yellow and coagulates spontaneously on removal.

DeWitt H. Sherman¹⁶ reports an instance of death from tuberculous meningitis in a breast fed infant 10 weeks old. The family history was negative in regard to tuberculosis. The child had never been on the street, had never had any food but breast milk, and no water which had not been boiled. He was taken ill suddenly with convulsions.

15. Leitch, D. B.: Xanthochromia of Spinal Fluid with Complete Coagulation in Tuberculous Meningitis, *Am. J. Dis. Child.* **15**:348 (May) 1918.

16. Sherman, H. DeWitt: Death from Tuberculous Meningitis in a Breast-Fed Infant at Ten Weeks of Age, *Arch. Pediat.* **35**:362 (Sept.) 1918.

developing ptosis of the right eye on the third day. When Sherman saw the child on the third day, the pupil of the right eye was larger than that of the left, and the pupillary reaction of both eyes was sluggish. There was some bulging of the anterior fontanel, and slight rigidity of the neck. The child could be aroused, but made no further response. Tubercle bacilli were found in the spinal fluid and inoculation tests into guinea-pigs proved positive. The child died on the seventh day of the illness.

F. van der Boget¹⁷ believes that tuberculous meningitis occasionally, though not frequently, ends in recovery, and reports a case in point. The patient was a child 3½ years old, and, when seen by the author, it had been ill eleven days with a rigidity of the neck which resembled torticollis. The symptoms on which a tuberculous meningitis was based were marked irritability and sensitiveness to external irritation, distinct rigidity of the neck, a temperature irregular in character, reaching 105 F. on several occasions and continuing for fifty-nine days, and the spinal fluid findings, namely, a lymphocyte count of 45 and the presence of tubercle bacilli. A guinea-pig inoculated with the fluid developed typical tubercular lesions. Improvement followed the second lumbar puncture, which was made a month after the onset of the disease, and recovery was uninterrupted. Van der Boget emphasizes the danger of giving the unfavorable prognosis usually given in these cases of tuberculous meningitis; he thinks this influences the family against repeated lumbar punctures, in which lies the only hope of recovery.

From a careful review of the literature, it appears that Van der Boget is correct in regard to the prognosis of tuberculous meningitis. The only patients who have recovered have been those treated by repeated lumbar punctures. V. Bokay collected a series of twenty-nine cases from medical literature, and added the reports of three of his own in which recovery followed this procedure.

According to P. H. Pierson,¹⁸ hemoptysis does not occur in more than 2 or 3 per cent. of tuberculous children. When it does appear as an early symptom, it is usually the result of pressure on and erosion of a blood vessel in the region of the hilus by enlarged or caseous lymph glands. Pierson reports five cases of hemoptysis in a series of 198 cases, seen in the Stanford chest clinic for children. Four of the five children had been exposed to tuberculosis; two were 5 years of age, one was 6 years old and two were 9 years old; four were girls and one was a boy. Physical signs and roentgen-ray findings corre-

17. Van der Boget, F.: Prognosis in Tuberculous Meningitis, *Arch. Pediat.* **35**:676 (Nov.) 1918.

18. Pierson, P. H.: Hemoptysis in Children, *Arch. Pediat.* **35**:527 (Sept.) 1918.

sponded very definitely. There was always present increased dulness over the hilus and an increase in harshness in the breathing. Of importance was a musical quality to inspiration and expiration, which denotes an active irritating process. The roentgenograms showed that these signs corresponded to the hilus thickening. Moreover, they showed the extent of the fine markings near the periphery and the dissemination or calcification of the lesions, as they progressed.

E. Bronson¹⁹ reports an instance in which a tuberculous pleural effusion supervened during an attack of erythema nodosum. The child was admitted to the hospital with lesions typical of erythema nodosum. The von Pirquet test was strongly positive. On the eighteenth day there was a rise in temperature, with a serous effusion into the pleural cavity, which later proved to be of a tuberculous nature.

Bronson, discussing the etiology of erythema nodosum, does not believe that it bears any relationship to rheumatism or that it is a specific fever. In this case the strong tuberculin reaction and the clinical association of the two conditions speak in favor of a tuberculous origin, but the comparative rarity of such association in hospital practice speaks against it. The etiology of erythema nodosum seems not yet to have been established.

G. Genoese²⁰ reviews the literature on chronic hemorrhagic purpura and reports two cases in children 6 and 2 years old, respectively, who soon after the appearance of the purpura developed pulmonary tuberculosis. He believes that the purpura was the first manifestation of the tuberculosis. He quotes Bensaude, who found seven cases of evident tuberculosis and five of probable tuberculosis among thirty-six cases of chronic purpura, and Monnot, who found sixteen cases of tuberculosis among forty-eight cases of purpura. Genoese calls attention also to the fact that giant ecchymoses sometimes appear under the influence of tuberculin treatment.

L. Petitpierre²¹ describes a form of acute tuberculous nephritis—which is not a manifestation of acute miliary tuberculosis. It occurs either in the course of a pulmonary tuberculosis or as a primary tuberculosis of the kidney. The onset is usually gradual, with symptoms which point to a disturbance of the gastro-intestinal tract or the onset may be sudden, with pain in the lumbar region, edema of the lower extremities and face, fever and albuminuria. Gastric disturbances are frequent. There is arterial hypotension and a polyuria which is con-

19. Bronson, E.: Erythema Nodosum Associated with Tuberculosis, *Brit. J. Child. Dis.* **15**:91 (April-June) 1918.

20. Genoese, G.: Chronic Purpura and Tuberculosis, *Riv. di clin. pediat.* **17**:304, 1919.

21. Petitpierre, L.: Acute Tuberculous Nephritis, *Arch. de med. d. enf.* **21**:467 (Sept.) 1918.

stant and of diagnostic import. Hematuria is persistent. A family history of tuberculosis is helpful in establishing the diagnosis, but it must be confirmed by finding the tubercle bacilli in the urinary sediment through staining methods or animal inoculation. A focal reaction after an injection of tuberculin is also confirmatory. The author's case is as follows: an 8 year old child was admitted to the hospital for acute hemorrhagic nephritis. Five months before albumin had been found in the urine and just before entrance albumin and blood were found. The mother was suffering from pulmonary tuberculosis. Examination showed a somewhat emaciated child, with impaired resonance and increased vocal fremitus over the right pulmonary apex. The heart was enlarged to the right and there was accentuation of the second aortic tone. The urine contained albumin and blood. The von Pirquet, Mantoux and Wassermann tests were negative. The albumin gradually disappeared but the blood persisted. Diuresis increased progressively, until the child was passing from 800 to 1,000 c.c. of urine in twenty-four hours. After three weeks in the hospital, there was an acute exacerbation. The albumin soon disappeared again, but the blood persisted. Two months after entrance, the child developed a phlyctenular keratoconjunctivitis. A diagnosis of tuberculous nephritis was based on the successive attacks of hematuria, the polyuria, the arterial hypotension, the finding of a pulmonary lesion, and the appearance of the phlyctenular keratoconjunctivitis. A year after entrance to the hospital, the urine was normal. The child was given 3 mg. of tuberculin, when albumin and blood at once appeared in the urine. The author's observations show that in considering the etiology of nephritis, tuberculosis must be kept in mind. Also the likelihood of recurrences in this form of nephritis must not be forgotten.

Petitpierre's report is of especial interest, as tuberculosis is not commonly considered a cause of hemorrhagic nephritis. This possibility may clear up the origin of an occasional obscure case.

J. C. M. Fournier²² reports an instance of Raynaud's syndrome in a tuberculous child. The patient, a boy, aged 12 years, was admitted to the hospital with evidence of tuberculous involvement of the right apex. Three weeks later there were well marked signs of meningitis. At the same time he developed a symmetrical asphyxia of the upper and lower extremities. Both hands and feet were cyanotic, cold, and painful. This condition gradually subsided but recurred to such a marked degree that gangrene of the limbs was feared. It again subsided, to recur still another time. The child died seven weeks after admission. Necropsy showed tuberculous meningitis, pleurisy, caseous areas in the lungs and caseous lymph nodes.

22. Fournier, J. C. M.: Raynaud's Syndrome in a Patient with Tuberculous Meningitis, *Abstr., Arch. de méd. d. enf.* **22**:438, 1919.

W. Stanley Gibson²³ has made a careful study of ninety-two cases of phlyctenular conjunctivitis. The investigation included an exhaustive history, a painstaking physical examination, and various laboratory tests, with special attention to the numerous views as to the cause of this condition which have been brought forward. Among these views the following were considered sufficiently important to merit separate discussion: (1) impairment of the general health; (2) bad living conditions; (3) gastro-intestinal disturbances; (4) the exudative diatheses; (5) tuberculosis.

Patients with phlyctenular conjunctivitis did not differ in regard to general health and development and the history of previous illnesses from those presented for other complaints. Bad living conditions were not frequently found, and the author thinks that they play a factor much less important in the production of this condition than is generally imagined. As to gastro-intestinal disturbances, the patients seemed particularly free from complaints referable to the gastro-intestinal tract. There were several typical examples of the exudative diathesis, and sometimes the presence of tuberculous cervical glands completed the picture of scrofula. But even to assume that phlyctenular conjunctivitis is a manifestation of the exudative diathesis would amount only to a restatement of the problem, for the cause of the so-called diathesis is altogether obscure.

The frequent occurrence of phlyctenular disease not only in scrofulous children, but also in those who showed other clinical types of tuberculosis suggested the possibility of the conjunctivitis resting on a tuberculous basis. A von Pirquet test was positive in all but two cases, and these were the only two cases in the series not typical of the disease. The author believes that the tuberculous theory of the etiology of phlyctenular conjunctivitis brings into harmony the other apparently conflicting opinions as to its cause. Impairment of the general health, bad living conditions, and insufficient food furnish favorable opportunity for tuberculosis to gain a foothold. Gastro-intestinal disturbance may be a symptom of obscure tuberculous infection. The exudative diathesis gives a soil favorable to the entrance and growth of the tubercle bacilli, which may then produce the clinical picture known as scrofula.

The author's experiments on rabbits also point to a tubercular origin of phlyctenular conjunctivitis. Phlyctenules were produced experimentally in tuberculous rabbits in eight instances, six times as a complication of conjunctival reactions resulting from the instillation of tuberculin, twice in the absence of local irritation of any kind. Numerous attempts to produce the condition in nontuberculous rabbits were unsuccessful. The pathology of the experimental lesions was similar

23. Gibson, W. Stanley: Etiology of Phlyctenular Conjunctivitis. *Am. J. Dis. Child.* 15:81 (Feb.) 1918.

to that of phlyctenules in human beings. The microscopic findings suggest a tuberculous origin. The author concludes that all clinical, experimental and pathologic evidence points to tuberculosis and tuberculosis alone as the cause of phlyctenular disease.

C. Combéléran²⁴ reports a case of tuberculosis of the vulva in a child 1 year old, whose mother had tuberculosis. According to the history given by the mother, the lesion on the vulva was preceded by swelling and the discharge of pus from the right inguinal glands. On examining the child, the author found an ulcer of a week's duration, which involved the right labium minorum and the right side of the fourchet. The base was of a pale rose color, with projecting whitish points about the size of pin points. In the right inguinal region was a broken down gland, and in the left inguinal region were two enlarged lymph glands. There were no physical signs in the lungs, but the child developed a cough and tubercle bacilli were found in the sputum. Microscopic examination of the tissue from the ulcer showed tuberculous changes. The ulcer was excised and curetted, but six months after the onset was still not healed.

The author collected thirty-seven cases of tuberculosis of the vulva from medical literature, and found that in most instances they were of primary origin. The diagnosis is sometimes difficult and often necessitates histologic examination.

F. Tits²⁵ describes tuberculosis of the middle ear. He says that infection rarely takes place through the drum membrane, that it usually travels from the nasal fossae or from the pharynx through the eustachian tube. Occasionally, in patients suffering from osseous tuberculosis it is carried through the blood stream. The chief form in children is the so-called necrotic form. It occurs in children who have not a severe tuberculous disease. It is characterized by an abundant discharge of fetid pus and early facial paralysis. The patients frequently complain of noises in the affected ear and of vertigo. Symptoms of acute mastoiditis usually occur, and death results from a meningitis. At other times, the disease runs a much slower course, with necrosis of the internal ear and fistula of the mastoid. The diagnosis is based on the general condition of the patient, the presence of visceral or osseous tuberculosis, the presence of multiple perforations of the drum, the resistance to all treatment, and the finding of tubercle bacilli in the aural discharge.

The possibility that a chronic discharge from the ear is of tuberculous origin should always be kept in mind by the pediatrician. It may lead to a diagnosis and the institution of proper treatment before the process has become too widespread to be influenced.

24. Combéléran, C.: Tuberculosis of the Vulva, *Internat. Clin.* **2**:158, 1918.

25. Tits, F.: Tuberculous Otitis Media, *Arch. méd. Belges* **71**:168 (Aug.) 1918.

TUBERCULOSIS OF THE TRACHEOBRONCHIAL AND CERVICAL
LYMPH GLANDS

L. J. Moorman²⁶ discusses tuberculosis in children, with special reference to tracheobronchial gland tuberculosis. He quotes Krause, whose recent experiments, he thinks, prove that the tracheobronchial glands may ultimately receive tubercle bacilli which have traveled from remote parts of the body and failed to find any demonstrable lodgment in the lungs. He does not agree with Ghon that all cases are air borne, with a primary focus in the lung and a secondary focus in the bronchial glands.

Moorman emphasizes the fact that the great majority of children are infected, and that the infection may at any time become a clinical tuberculosis. He asserts, too, that the first symptoms are those of a toxemia, namely, weakness, undue fatigue, poor appetite, failure to gain in weight and nervous irritability. This group of symptoms becomes particularly significant when there is a history of contact with tuberculous individuals, or when there are signs of local involvement, such as cough and hoarseness. In these instances a thorough examination of the chest should be made, with special reference to interscapular dulness and the presence of d'Espines sign. Diminution in the intensity of breath sounds on the side of greatest involvement is suggestive, and is probably due to pressure from enlargement of the hilus group of glands. The roentgen-ray examination is important, but the results must be interpreted in the light of the history and physical examination. The von Pirquet test is of value in diagnosis but must be repeated two or three times before it can be considered as being negative.

Moorman examined 135 children at the Oklahoma City Tuberculosis Dispensary. Of these, fifty gave a history of exposure to open cases, seventy were exposed to suspected cases and fifteen gave no history of exposure. A history of the following symptoms was obtained: cough in 59 cases; expectoration in 29; pain in chest in 24; pleurisy in 14; hemoptysis in 2; night sweats in 11; loss of flesh in 25; loss of strength in 34; hoarseness in 17; fever in 19; loss of appetite in 28; disturbed digestion in 27. Physical examination revealed the following: weight below standard, 73; height below standard, 17; general appearance good in 95, fair in 48, poor in 21. Type of chest normal in 121, abnormal in 14, dulness elicited by percussion in 89; d'Espine's sign was present in 35; râles in 29. Sixty-nine children were examined roentgenographically and the roentgenogram showed tuberculosis of the tracheobronchial glands alone in 11 cases; tuberculosis of the tracheobronchial glands with peribronchial thickening in 29 cases; tuberculosis

26. Moorman, L. J.: Tuberculosis in Children with Special Reference to Tracheo-Bronchial Gland Tuberculosis, *Oklahoma M. A. J.* **12**:123 (May) 1919

of the tracheobronchial glands and peribronchial thickening with involvement of the lung tissue in 19 cases; nontuberculous infection in 3 cases. The diagnosis as recorded in the 135 cases was: tuberculosis of the hilus alone in 34 cases; tuberculosis of the hilus with peribronchial and lung involvement in 44 cases; doubtful, 40 cases; cases with nontuberculous infection, 5; negative, 12 cases.

J. C. McGowen²⁷ describes the clinical and roentgen-ray diagnosis of bronchial gland tuberculosis. He says that loss of weight, combined with a dry, hacking cough, paroxysmal in character, with frequent recurrences at night, are suspicious symptoms. Attacks of pain in the region of the heart without apparent cause, occasionally accompanied by a fit of coughing, are produced by compression of the vagus nerve by enlarged bronchial glands.

Enlargement of the glands of the neck and supraclavicular spaces are often associated with bronchial gland infection, as are also enlargement and swelling of the superficial veins of the chest. Dulness in the oval space on each side of the second, third and fifth dorsal vertebrae is significant, but is not caused by the glands themselves but by interference with lines of communication to the surface structure by the glands. Dulness over one or both apices and in the oval space, with localized and persistent fine crepitant râles, is almost conclusive evidence of the presence of active tuberculous disease.

McGowen thinks that roentgen-ray examination gives more valuable evidence as to the presence of tuberculosis than physical examination, but it gives no proof of the activity of the disease.

In early tuberculous disease in children, when either the bronchial glands or the lung tissue are involved, there is an increase in the normal hilus shadows, especially on the right side. The trabeculae of the lung are thickened, and, if the disease has progressed to any extent, irregular, circular patches are seen in the pulmonary parenchyma.

E. Schmieglow²⁸ remarks that perforation of tuberculous glands into the air passages or the esophagus has often escaped detection during life, and necropsies have shown that this was a cause of death from suffocation. He says that it is possible by modern methods to determine whether enlarged bronchial glands are responsible for stenosis of the air passages and to anticipate this catastrophe. Schmieglow tabulates twenty cases of perforation of the bronchial glands into the bronchi which he collected from the literature, and reports a number which have come under his own observation. He says that symptoms of compres-

27. McGowen, J. C.: Early Diagnosis of Tuberculosis in Children, *Brit. J. Tuberc.* **12**:145 (Oct.) 1918.

28. Schmieglow, E.: Tuberculous Bronchial Gland, *Hospitaltid.* **61**:129 (Jan. 30); 161 (Feb. 6) 1918; *Abstr., Am. Rev. Tuberc.* **2**:581, 1918.

sion by enlarged glands are: expiratory dyspnea, a cough which resembles whooping cough and occurs spasmodically, an area of dullness in the interscapular region and a peculiar whistling character of the respiration. When suppuration and perforation into the bronchus occurs, the child may cough up the softened gland, but often it is too large, and suffocation results if operative procedures are not resorted to. Symptoms of stenosis are an indication for bronchoscopy and it may be possible to aspirate the contents of the gland through the bronchoscope. When the enlarged glands are in the anterior mediastinum, they can only be reached by removal of the sternum. Tracheoscopy is especially useful in cases which develop gradually. In children under 6 years of age, it is necessary to perform a tracheotomy before tracheoscopy, but not in older children.

The following standards²⁹ of diagnosis and treatment of tuberculous cervical adenitis have been prepared by the National Tuberculosis Association: Enlarged cervical glands in children under 2 years of age are usually due to some acute inflammatory process rather than to tuberculosis. Any well marked enlargement of the anterior cervical glands, that persists for several months after throat and mouth infections have been relieved, should be considered tuberculous. Tuberculosis should be considered seriously as a cause of enlarged cervical glands when there has been known exposure to tuberculosis from human or bovine sources. Enlargement of cervical glands may take place following or during acute infectious diseases of childhood, acute or chronic tonsil infections, pharyngitis, carious teeth, leukemia, Hodgkin's disease, syphilis, middle ear disease, eczema, mycosis or irritation of the scalp. Enlargement of the glands posterior to the sternomastoid are usually nontuberculous. Tuberculosis should be considered seriously if constitutional signs and symptoms, such as anemia, malnutrition, fever, rapid pulse, loss of weight and strength, accompany enlarged cervical glands. Tuberculosis should not be considered the cause, unless the enlargement has persisted for several months, but it is a safe rule, after having to discard other diagnosis, to regard as tuberculous any gland which has been enlarged for three months or more. In the presence of evident focal infections, as diseased tonsils or adenoids or carious teeth, it is better to take it for granted that such glands are not tuberculous, until the effects of the removal of the tonsils and adenoids and the clearing up of the teeth has been observed. A pathologic examination of a portion of gland should be made if there is any doubt as to the diagnosis, and the removed tonsil should

29. Standards of Diagnosis and Treatment of Tuberculous Cervical Adenitis, *Am. Rev. Tuberc.* 2:565, 1918.

be examined for tuberculosis histologically and by animal inoculation. Confirmatory evidence of the tuberculous nature of the enlarged glands may be secured through the tuberculin test and the roentgen ray, and in manifest tuberculous conditions in other parts of the body.

Tuberculous cervical adenitis should always be treated as a general disease with local manifestations. All possible portals of entry of infection, such as teeth, nasopharynx, tonsils, ears and scalp should be examined and all infections treated. All methods of treatment should be considered carefully in each individual case, and whatever line of treatment is instituted, hygiene should play a most important part. Tuberculin, surgery, heliotherapy, and the roentgen ray may be valuable in the treatment of tuberculous cervical adenitis, but only when associated with hygienic treatment.

R. S. Haynes³⁰ says that an adenitis in a child under 2 years of age is likely to be a simple rather than a tuberculous inflammation; when the child is over 2 years of age, it is more likely to be tuberculous; but widespread tuberculous adenitis may occur in susceptible infants. A knowledge of the diet, of the milk used and of the child's surroundings, is important in diagnosis. A negative history of contact is more important than a positive one. According to Haynes, tuberculous adenitis is rarely acute. A slow increase of the swelling, with gradual involvement of more than one node, and delayed involvement of the skin and deeper structures speaks for tuberculosis. In early infancy, however, a rapid and acute onset may characterize tuberculous swelling and cause difficulty in diagnosis. When an enlargement has lasted more than three months, the process is probably tuberculous, although in infancy mild simple infections may run such a course. The presence of a single, slowly enlarging node, particularly if it is a tonsillar node, points to tuberculosis. Simple adenitis usually presents a fairly early stage enlargement of several nodes; tuberculous adenitis shows in a late stage enlargement of several nodes. Inflammation of the structures in the mouth, throat and nasopharynx points to the diagnosis of simple or pyogenic, rather than tuberculous enlargement of a node. A persistent discharging sinus points to a tuberculous infection. Examination of the blood shows a polynucleosis in the pyogenic enlargements and a lymphocytosis in the tuberculous enlargements, but secondary infection in tuberculous adenitis also causes a polymorphonuclear leukocytosis. A negative von Pirquet test is valuable evidence of a pyogenic infection. The author emphasizes the difficulty of diagnosis and frequently finds it necessary to excise and examine a gland before definitely determining it.

30. Haynes, R. S.: Diagnosis of Enlarged Lymph Nodes. *Arch. Pediat.* **35**:226 (April) 1918.

DIAGNOSIS

M. Fishberg³¹ criticises the standards of diagnosis of pulmonary tuberculosis in children issued by the National Association for the Study and Prevention of Tuberculosis. In the first place, he does not think that such a polymorphous pathologic process as tuberculosis can be standardized. He points out that malnutrition, on which much emphasis is laid, may be caused by other factors than tuberculosis, that pleurisy is not always of tuberculous origin in children; that lassitude and fretfulness, symptoms attributed to tuberculosis, are the usual symptoms of a lymphatic diathesis; that night sweats are seen in physically healthy children and are significant only when they occur in the early morning hours. He points out that an elevation of temperature in children is not a positive indication of a serious process. With regard to physical signs, he takes issue with the statement that râles occur infrequently in the apices and along the border of the sternum. In cases of pulmonary tuberculosis in children, Fishberg has always found râles in the apices. He emphasizes that the time has passed when a positive tuberculin reaction was sufficient as a basis for a diagnosis of tuberculous disease, even in a child with some of the above symptoms and signs. In regard to the statement that pulmonary tuberculosis should be suspected in patients with glandular, osseous and articular tuberculosis, Fishberg states that pulmonary tuberculosis is exceedingly rare in individuals of any age who are suffering from these forms of the disease. He takes exception also to the statements that on an unexplained hemoptysis, with a positive tuberculin reaction, with or without a definite positive roentgenogram, a diagnosis of pulmonary tuberculosis is to be made, and given a roentgenogram which shows unmistakable mottling, with a positive tuberculin reaction in a child under 3 years of age, even if constitutional symptoms are absent, the diagnosis of pulmonary tuberculosis is to be made. He thinks that expectoration of blood comes usually from enlarged tonsils and adenoids, and that a roentgenogram of a child over 4 years of age, which shows no mottling or opacities in the region of the hilus, is very rare. Fishberg has seldom encountered pulmonary tuberculosis in children between 4 and 12 years of age, but he has seen many cases of tracheo-bronchial adenopathy in children, and is surprised that this form of tuberculosis is not even touched on in the standards laid down by the committee.

31. Fishberg, M.: A Criticism of the Standards of Diagnosis of Pulmonary Tuberculosis in Children Issued by the National Association for the Study and Prevention of Tuberculosis, New York M. J. **106**:967 (Nov. 24) 1917.

J. Hess³² discusses the various tuberculin skin reactions in children. These are divided into qualitative and quantitative tests. The simplest of the qualitative tests is the von Pirquet. Hess describes six types of reaction following the von Pirquet test: (1) The usual typical tuberculin reaction, which begins within four or six hours, reaches its maximum in from twenty-four to thirty-six hours, and then rapidly fades, although infiltration persists for several days. (2) A premature reaction, characterized by rapid evolution and slight intensity. (3) A persistent reaction, which reaches its maximum slowly and then remains unchanged for a week or longer. (4) A late reaction, which makes its appearance after an incubation period of more than twenty-five hours. (5) A cachetic reaction, characterized by infiltration with little or no redness. (6) A scrofulous reaction in which there are one or more papules, surrounded by a painful area of redness from 5 to 10 cm. in diameter.

Quantitative tests, according to Hess, are of little practical value. The intercutaneous test is the one most extensively used. Hess makes four simultaneous injections, (a) 1/20 c.c. of salt solution as a control, (b) 1/20 c.c. of a 1:1,000,000 solution of tuberculin, which equals 0.00005 mg.; (c) 1/20 c.c. of a 1:100,000 solution, or 0.0005 mg.; (d) 1/20 c.c. of a 1:10,000 solution, or 0.005 mg. If there is no reaction, he uses 1/20 c.c. of a 1:1,000 dilution, or 0.05 mg. and 1/20 of a 1:100 dilution, or 0.5 mg. When the test is positive, a pink infiltration appears within several hours, increases during the first twenty-four hours, and attains its maximum on the second day. This test has four advantages over the von Pirquet, the more exact dosage, the earlier reaction, the more distinct reaction and its greater reliability, because of certainty of absorption of the tuberculin. The subcutaneous and percutaneous tests are less extensively used. Hess agrees that the tuberculin skin reaction is a specific reaction. It gives indication of present or previous tuberculous infection, but not necessarily of active tuberculous disease. The quality of the reaction is of little importance for the diagnosis of the intensity of the process. A negative reaction to the von Pirquet cutaneous tuberculin test, especially if made twice, occurs only in individuals entirely free of tuberculosis or in individuals suffering from acute infectious disease, during pregnancy, after introduction of large doses of tuberculin, in cachetic conditions and in advanced and miliary tuberculosis. Hess believes that the tuberculin reactions should be considered as adjuncts to careful clinical examination and observation, and not as a definite means of diagnosis or as establishing a prognosis.

32. Hess, J. H.: Tuberculin Skin Reactions in the Diagnosis of Tuberculosis in Children, *Med. Clinics N. America* 1:1357, 1918.

E. F. Warner³³ has selected the subcutaneous, the von Pirquet, the Mantoux, and the Ellis papillary cutaneous tuberculin tests as the most practical for use in children. He thinks that the subcutaneous is one of the most valuable, and that it is too much neglected by pediatricians, on account of the time it involves and the unfounded fear of violent reactions. A positive von Pirquet simply implies that the child has at some time become infected with tubercle bacilli. The greatest value of the intradermic test is to determine the degree of hypersensitiveness of patients with active tuberculosis, in order to regulate the dose of tuberculin with which to commence treatment.

Warner believes that the Ellis multiple papillary cutaneous test is the most valuable for separating the active from the latent cases. The test is performed as follows: Scarifications are made with an ordinary vaccination lancet through each of seven drops of solutions of tuberculin placed in a row on the inner side of the forearm. Scarifications must open the papillary layer of the skin, to draw blood. The solutions used are bovine tuberculin, full strength, for mark 1. The other five solutions are made from old tuberculin of the human type. For mark 2 a 1:10 solution is used; for mark 3, a 1:100 solution is used; for mark 4, a 1:500 solution is used; for mark 5, a 1:1,000 solution is used; for mark 6, a 1:10,000 solution is used; mark 7 is used as a control. A high colored, edematous reaction denotes an active lesion, a dark colored reaction denotes an old or quiescent lesion, if it is nearly black, with no swelling, the patient's condition is hopeless. No reaction is shown in a far advanced case. Incipient cases yield a reaction to mark 1 or 2. Probably, if there was a reaction to mark 6, the amount of lung tissue involved in the tuberculous process would be a very small patch, just definitely detectable by the stethoscope. The usual moderate lesions give reactions on mark 3 or 4. A reaction on mark 3 is the most important for the pediatrician, as it is the dividing line between active and latent lesions.

In twenty-three Ellis tests, Warner obtained ten positive reactions to mark 4, three to mark 3 and ten negative reactions. The results in this small series show only three active cases out of twenty-three, or a little more than 10 per cent. The author thinks further investigations by means of a reliable tuberculin test should be undertaken to separate active from latent cases of tuberculosis.

There seems to be considerable difference of opinion in regard to the relation of the severity of the cutaneous tuberculin reaction to the activity of the tuberculous process. Most writers believe little can be

33. Warner, E. F.: A Comparison of the Various Tuberculin Tests in Childhood, *Arch. Pediat.* **35**:28 (Jan.) 1918.

told from the type of the reaction. Perhaps Warner's report will stimulate more investigations along these lines and his conclusions will be proved to be accurate.

E. M. Sill³⁴ subjected 658 children, ranging in age from 2 months to 13 years, to the von Pirquet test. The children were the average type of the lowest East side of New York. The parents were mostly of foreign birth, but in no case was there a family history of tuberculosis. A positive reaction was found in sixty-one or 9.2 per cent., figures, which seem to give a fair estimate of the frequency of infection with tuberculosis in children with healthy parents in New York City. Sill thinks that in young children a positive reaction indicates a recent infection that is active or partially healed, while in older children the intensity of the reaction indicates the hypersensitiveness of the child, rather than the degree of the disease. When the reaction comes on quickly, it means an active focus; a slow or delayed reaction means a latent focus. Some children do not react to the first dose, but they do react to the second test. Comparing the results of the present investigations with others, the author concludes that the incidence of tuberculosis infection in children varies not only in different countries but in different states of the United States, and varies also among children in hospital and clinic practice.

M. H. Bass³⁵ is of the opinion that, in spite of the advance in knowledge, there is still a great deal to be learned about the tuberculin reaction as it affects children. He was led to collect data on this subject by the fact that he found in an asylum a number of children with negative reactions, who had reacted positively six months before. In many of the children the test was repeated several times in the course of a few days, and the reaction was changed from negative to positive. Bass then thought that by repeatedly testing a large number of infants and young children, latent tuberculous infection would often be revealed. The following procedure was carried out. Each child was subjected to a von Pirquet test, observed after twenty-four and again after forty-eight hours. A positive reaction was regarded as evidence of tuberculous infection. If the test was negative, a second von Pirquet test was performed, and a third, if necessary. If these tests were both negative, an intradermic injection of 0.1 c.c. of 1:1,000 of old tuberculin (0.1 mg.) was given. If this was negative after forty-eight hours, 0.1 c.c. of a 1:100 solution (1 mg.) was injected and repeated after forty-eight hours if the result was still negative. If after these six tests the child still failed to react, he was considered definitely negative.

* 34. Sill, E. M.: The von Pirquet Reaction in Children, New York M. J. **107**:1018 (June 1) 1918.

35. Bass, M. H.: Cutaneous and Intercutaneous Tuberculin Tests in Infants and Children, Am. J. Dis. Child. **15**:313 (May) 1918.

In all, 1,165 tests were made on 206 children, varying in age from a few days to 6 years. Fifty-two children showed a positive reaction to some of the tests, or 25.2 per cent. If only one or two tests had been made, incorrect conclusions would have been drawn as to the number of children infected. It was interesting to note the steplike increase in the disease incidence, with increasing age. Out of fifty-one children under 6 months of age, four reacted positively, or 7.8 per cent. Of children in the second 6 months, 15.8 per cent. were positive; of those from 1 to 2 years old, 17.2 per cent. were positive; of those from 2 to 3 years old, 31.3 per cent. were positive and, finally, of the children between 5 and 6 years old, 78 per cent. were positive.

The author's results emphasize the fact that any series of examinations designed to ascertain the incidence of tuberculous infection must consist of more than a single test in each case. They show the great frequency of positive reactions in children.

Bass's report is timely, and emphasizes the importance of repeating the tuberculin test before the patient is pronounced free of tuberculosis.

J. P. Garrahan and L. Iraola³⁶ attempted to ascertain the frequency of latent tuberculosis in children. They examined 1,214 children from poor homes and two orphan asylums at Buenos Aires and found that 75 per cent. of the children, even though apparently healthy, responded positively to tests for tuberculosis. The proportion of positive reactions was 20 per cent. less among the children who had lived all or part of their life in the asylum than among the children who lived at home.

L. M. Spolverini³⁷ has made a study of latent tuberculosis in infants. He applied the tuberculin tests to 900 supposedly nontuberculous children under 1 year of age, and obtained a positive reaction in 63, or 7 per cent. Of the eight infants, 3 or 4 months old, he obtained reactions in only 0.80 per cent.; of twenty-two infants from 4 to 6 months old, 2.44 per cent. reacted, and of thirty-three infants from 5 to 12 months old, 3.66 per cent. reacted. The writer emphasizes again that contagion in the family is most likely to be the source of infection in infants, and that the first apparent localization of the disease is in the tracheobronchial glands.

A. Arnfinnsen³⁸ tested 7,969 school children with the von Pirquet tuberculin test. He obtained a positive reaction in 37.8 per cent. of

36. Garrahan, J. P., and Iraola, L.: Latent Tuberculosis in Children, *Rev. méd. del Uruguay* **22**:459 (June) 1919.

37. Spolverini, L. M.: Latent Tuberculosis in Infants, *Riv. di Clinica Pediat.* **17**:169, 1919.

38. Arnfinnsen, A.: Tuberculin Skin Tests in Children, *Norsk Mag. f. Lægevidensk.* **80**:508 (May) 1919.

the 6,978 children attending the public schools and in 33 per cent. of the 991 children attending private schools.

E. Friedman³⁹ performed the von Pirquet test on 464 children of Colorado. The desire to ascertain in what manner the climate of Colorado modifies tuberculous infection and tuberculous disease in children was responsible for the work. Nearly all the children tested were living under conditions comparable with those prevailing among the poorer working classes of the large cities. Most of the children were of tuberculous parents, many of whom had been inmates of sanatoriums, where they had had thoroughly inculcated rules of prophylaxis.

Of the 464 children tested, 39.8 per cent. reacted, and the number of positive reactions among the males was 2 per cent. greater than in the females. Of children less than 1 year of age, almost 12 per cent. reacted positively; from 10 to 14 years, 55 per cent. reacted positively, and from 14 to 18 years only 51 per cent. reacted positively. The highest number of positive reactions was noted from the eleventh to the thirteenth year. These figures do not show the uniform increase from year to year in the percentage of positive reactions which characterize the findings of other writers, and Friedman is at a loss adequately to account for this deviation.

The author found that of children not exposed to tuberculosis, less than one half as many react than of those exposed, but he did not find that children exposed to a closed case of tuberculosis reacted less frequently than those exposed to an open case. He was not able to corroborate the statement that tuberculous infection exercises a retarding influence on physical growth, or that there is a causal relation between measles and whooping cough and tuberculous infection.

Friedman draws the following conclusions from his study: The climate of Colorado exercises no striking influence in the prevention of tuberculous infection in children of tuberculous parentage. Among the nonexposed children, however, the frequency of infection is comparatively lower than obtains elsewhere. Active tuberculosis is conspicuous by its infrequency, and, when it occurs, it is exceedingly mild, with a tendency to prompt and complete healing. Among Colorado children fatalities to be ascribed to tuberculosis are so rare as to be negligible. This infrequency of tuberculous infection in Colorado born children, the tendency to localization and to rapid recovery in the event of activity, and the low death rate all testify to the beneficial effects of the Colorado climate on the prevention and arrest of tuberculosis in childhood.

39. Friedman, E.: The von Pirquet Test and Results of Its Use in Four Hundred and Sixty-Four Cases, *Colorado Med.* **16**:246 (Oct.) 1919.

G. H. Cattermole ⁴⁰ made the tuberculin skin test on 419 children. Of 165 private patients, 42 per cent. gave a positive reaction and 58 per cent. gave a negative reaction; of 254 charity patients, 50 per cent. gave a positive reaction. Of the 254 charity patients, 167 were children treated at the University Dispensary, and eighty-seven came from an orphan home. Of the first group, 53 per cent. were negative, even though a large number of these children came from families where there were one or more cases of tuberculosis. In the second group, 57 per cent. gave a positive reaction. This was the highest percentage of positive reactions obtained in any group of children. At first, it seemed quite remarkable, as these children appeared to be well nourished and in better than average health, but the explanation lay in the fact that they came from homes in which one or both parents had died of tuberculosis.

In the children with positive reactions a healthy appearance is the rule. Ordinarily, they have but few signs in the chest, but when they contract any infectious disease the signs become apparent and persist for a longer time than in normal children.

The attempt to get a history from all children tested was successful in 202 cases. Of 101 children who gave a positive reaction, ninety-two had been exposed to tuberculous parents; sixty-one had been exposed to infection. This is a little more evidence that exposure in the home is the chief cause of tuberculous disease in children.

H. Heiman ⁴¹ has attempted to determine the value of the fixation reaction for the diagnosis of tuberculosis among infants and children. The blood serum of fifty patients, ranging in age from 6 months to 12 years was tested. Seventeen children were tuberculous, five were considered as being probably tuberculous or at least open to suspicion, and twenty-eight were nontuberculous. Among the tuberculous group were six cases of tuberculous meningitis, seven cases of pleural effusion, six cases of pulmonary tuberculosis, one of peritonitis, one of adenitis and one of tabes mesenterica. The complement fixation tests for tuberculosis on the serums of seventeen tuberculous infants and children with Miller's and Petroff's antigens gave one 4 plus, one 2 plus and two suspicious reactions. Complement fixation tests on the serums of five children, probably but not definitely tuberculous, were all negative with both antigens. Complement fixation tests on twenty-eight nontuberculous children gave three 4 plus and two suspicious reactions. In view of the very favorable reports given by others with the same anti-

40. Cattermole, G. H.: Tuberculosis in Children, *Northwest Med.* **15**:362, 1917.

41. Heiman, H.: The Complement Fixation Test for Tuberculosis in Infancy and Childhood, *Arch. Pediat.* **36**:32 (Jan.) 1919.

gens in general groups of individuals, Heiman would like to learn the experiences of others in this field, before discarding the test for children.

A. Reis⁴² has attempted to verify the findings of Bath that there is a direct relationship between the tuberculin reaction and the chest circumference and height of the child. Of 125 children from 3 to 10 years of age, eighty-four boys and forty-one girls, thirty-six gave a positive reaction. Of these, twenty-one were below the normal height, fourteen had a smaller and five had a greater chest circumference than normal. Reis concludes from his study that there is no relation between the von Pirquet tuberculin test and the height, but children who have chest circumferences below normal show a larger percentage of positive reactions than do those who measure up to normal.

Mary E. Lapham⁴³ has made a study of the roentgen-ray findings of the chests of 150 children in order to ascertain how often are found in the lungs structural changes resembling those found in the chests of tuberculous children. Four groups of structural changes were found: (1) moderate enlargement of the bronchial glands, with little or no infiltration of the lungs; (2) enlargement of the bronchial glands, with beginning infiltration of the lungs; (3) considerable enlargement of the glands with marked infiltration of the lungs; (4) changes typical of tuberculous conditions. Although none of the children had the clinical features of tuberculosis, many had changes typical of the disease, which could be detected by the roentgen-ray. Lapham concludes from these roentgen-ray studies that tuberculous processes originate in the bronchial glands and extend from them into the lungs; that enlarged bronchial glands and thready infiltration of the lungs occur commonly in children, but that their presence need not be associated with the disease called tuberculosis. They occur whenever secondary complications take place in the terminal areas of the bronchi. Structural changes in the lungs, detected either on roentgenograms or by physical signs or by both, do not warrant the diagnosis of tuberculosis as a disease. Lapham feels that a more intensive study of changes in the nerves and the ductless glands, due to tuberculous toxemia, is necessary before all deviations from health, which may represent a tuberculous etiology, can be recognized. She believes that many of the functional diseases of children are manifestations of an occult tuberculosis.

The value of the roentgen-rays as an aid to diagnosis must not be underestimated, but, as Lapham points out, there are other conditions which cause pulmonary shadows very similar to those caused by tuberculosis. Especially since the epidemic of influenza, 1918-1919, one

42. Reis, A.: Relation Between Height and Chest Measure and Tuberculin Reaction, *Arch. de méd. d. enf.* **21**:26 (Jan.) 1918.

43. Lapham, M. E.: Tuberculosis and Roentgen-Ray Plates, New York M. J. **107**:294 (Feb. 16) 1918.

finds shadows in roentgenograms which undoubtedly a few years ago would have been attributed to tuberculosis, but which are due to the influenza capillary bronchitis and bronchopneumonia and the resulting enlarged bronchial glands. Moreover, if too much reliance is placed on the roentgenograms there is a tendency to make a less painstaking physical examination and to forget many of the signs which aided clinicians to arrive at a diagnosis long before the advent of the roentgen-ray.

A. A. R. Green ⁴⁴ compared the physical signs in forty cases of early suspected pulmonary tuberculosis with results found on examination by the fluorescent screen. He says the points to which attention should be paid in screening a chest in a suspected case of tuberculosis are as follows: 1. The condition of the apices as regards translucency and the degree of illumination on coughing. 2. The condition of the structures at the hilus, whether, if the hilus is wider than usual, the enlargement is uniform in type or netlike, whether there are calcified areas or fibrous processes extending peripherally into the lung tissue. 3. Haziness, circumscribed or diffuse, of the lung tissue. 4. the movement of the diaphragm.

Green thinks, when physical findings are at variance with the roentgen-ray findings, greater stress should be laid on the second point. His reasons for this are that the sound-conducting power and resonating property of muscle vary with its tone, but the permeability of muscle to the roentgen-ray is usually the same. It is true, too, that deep seated areas of deficient aeration may be out of reach of percussion, yet may show almost as clearly on roentgen-ray examination as though they were on the surface.

L. Ribadeau-Dumas ⁴⁵ gives a detailed description of the roentgen-ray findings in pulmonary and glandular tuberculosis among infants and young children, and lays stress on their value as a diagnostic aid. Roentgenograms of pulmonary glandular tuberculosis in infants show at the base of the lung, a little above the diaphragm, a triangular shadow with its base toward the axilla. The apex meets the apex of another shadow, whose base corresponds to the mediastinum. The first shadow represents the perituberculous congestion around the initial lesion, the second, the enlarged bronchial glands. The evolution of the disease can be followed with the roentgen-ray. In cases which progress favorably, the shadow of the perituberculous congestion disappears, but that of the tracheobronchial glands becomes more prominent. Still later,

44. Green, A. A. R.: Comparison of Physical Signs in Early or Suspected Pulmonary Tuberculosis with Results Found on Examination by the Fluorescent Screen. *Brit. J. Tuberc.* **12**:153 (Oct.) 1918.

45. Ribadeau-Dumas, L.: Roentgenology of Tuberculosis. *Progrès méd.* **34**:372 (Sept. 20) 1919.

when the shadow of the perituberculous congestion disappears entirely, a small opaque area, which represents the remains of the primary focus, can be seen near the center of the posterior border of the axilla. In unfavorable cases the roentgenogram show extension of the primary focus. Sometimes the primary focus is never found, and only shadows of enlarged bronchial and pulmonary glands appear on the plate. Shadows of bronchial glands are seen most frequently on the right side. They represent either extrapulmonary or intrapulmonary glands. The extrapulmonary glands are those surrounding the trachea and bronchi, and the shadows extend from the base of the heart to the superior orifice of the thorax. Intrapulmonary glands cause shadows which sometimes are difficult to distinguish from hilus gland shadows. At other times they cause shadows radiating toward the periphery of the lung, in the region of the bronchi and blood vessels.

A. Weil ⁴⁶ says that the roentgen-rays should be used as an aid to diagnosis, not to establish a diagnosis. Important findings in the roentgenograms are: 1. Diminished transparency of the pulmonary apices. 2. Diffuse shadows in the region of the hilus. 3. Diminution of the excursion of the diaphragm on the affected side. 4. Lessened expansion of the thoracic wall, with sinking in of the ribs. 5. Lengthening out of the cardiac shadow.

P. W. Roberts ⁴⁷ says that until recently the diagnosis of tuberculous joint disease was considered one of the simplest and most definite problems with which the orthopedic surgeon is confronted, but from his studies on congenital syphilis, pursued during the last two years, he thinks that this simplicity is merely apparent. His records of more than 100 cases collected during the last two years give proof that a similar symptomatology may be produced by tuberculosis and inherited syphilis, and the roentgenographic findings show no differentiating characteristics. The Wassermann reaction in the present state of development is frequently negative in the presence of a direct family history of syphilis and there is no reliable laboratory test for tuberculosis, but fortunately nearly every case of joint disease due to inherited syphilis will, on exhaustive research, reveal some remaining imprint of the previous activity of the disease. The author lays special emphasis on the examination of the teeth in the differentiation of syphilitic from tuberculous joint disease. The deciduous teeth, the first permanent molars and incisors, are the ones which are most likely to show evidence of syphilis. The two conditions which the author finds most characteristic of syphilis are the widely spaced incisors and the "humpy

46. Weil, E. A.: Roentgen-Ray Signs of Tuberculosis, *Paris méd.* **8**:190 (March 2) 1918.

47. Roberts, P. W.: Syphilitic Joint Disease Simulating Tuberculosis, *J. A. M. A.* **70**:372 (Feb. 9) 1918.

molars," a term he uses, when there are alterations in the normally smooth lingual surface of the crown. In addition, he describes other alterations, early decay of both the first and permanent sets, the retention of deciduous units long after the period when they are usually displaced, and microdentition, as associated with congenital syphilis.

PROGNOSIS

L. Ribadeau-Dumas ⁴⁸ and H. Bécélère report a case of recovery from pulmonary tuberculosis in a child 13 months old. At the age of 9 months the child was put in the care of a nurse with an active tuberculosis. At 13 months he began to loose weight and had a slight elevation of temperature. A month later examination showed absolute dullness with disappearance of the normal vesicular breath sounds over the entire right side. The temperature elevation persisted for three weeks, when the area of dullness gradually diminished. The infant was very emaciated, had attacks of coughing, which resembled whooping cough, and a positive tuberculin test. There were also physical signs of enlarged tracheobronchial glands.

The child recovered, and the author had an opportunity to examine him six years later. There were no abnormal signs on examination of the chest, but the roentgen ray showed in the fifth interspace in the right posterior axillary region a small triangular shadow, probably a calcified tubercle, as well as small round shadows at the hilus (bronchial glands).

A. Grismondi ⁴⁹ discusses the papulonecrotic tuberculid and its grave prognostic significance. The literature cited the outcome in each case when this form of tuberculid is present. Papulonecrotic tuberculids occur on the back, buttocks and limbs. In none of Grismondi's cases did an attack of measles precede their appearance, though this has been reported by other observers. In one case, however, a post-scarlatinal broncho-pneumonia accompanied a widespread eruption of tuberculids. Grismondi calls attention to the fact that papulonecrotic tuberculids may be the only sign of tuberculosis, and that their presence may clear up many a puzzling diagnosis.

PROPHYLAXIS

A. F. Hess ⁵⁰ points out that statistics of infant mortality showing the ratio of deaths from tuberculosis as compared to deaths from other diseases do not give a true conception of the importance of tuberculosis at this period of life. To arrive at a better understanding of this

48. Ribadeaux-Dumas, L., Bécélère, H.: The Initial Lesion in Pulmonary Tuberculosis in Infants, *Bull. et mém. Soc. méd. d. hôp.* **43**:561, 1919.

49. Grismondi, A.: Tuberculids in Diagnosis and Prognosis of Tuberculosis in Children, *Pediatrics* **26**:635, 1918.

50. Hess, A. F.: The Significance of Tuberculosis in Infants and Children and Measures for Their Protection, *J. A. M. A.* **72**:83 (Jan. 11) 1919.

problem, figures must be prepared which show the absolute number of deaths annually. It is seen that in no one year do the deaths from tuberculosis exceed those of deaths occurring during the first year of life. This great loss is due, in part, to the peculiar susceptibility of infants, in part, to the fact that they receive an exceptionally large amount of the infective agent. Bovine infection plays a part that is minor but not negligible. In view of the not inconsiderable mortality that has been shown to be occasioned by the bovine type of bacillus, it would be well if cultural studies of tuberculosis in infants should be carried out from time to time, in order to gain an insight into the degree to which milk employed for infant feeding is contaminated by virulent tubercle bacilli.

Following the period of infancy, there is a quiescent phase in the mortality from tuberculosis, throughout which the deaths decrease year by year, although the number of infections, as shown by the tuberculin reaction, steadily increases. These infections are due probably to latent carriers, to individuals who from time to time shed tubercle bacilli. A daily examination of the sputum of a series of individuals, carried out carefully for a period of months, might well be undertaken in order to test the validity of this hypothesis.

There is a second active phase in connection with the mortality from tuberculosis. This is commonly associated with the third quinquennium of life. If the deaths are studied year by year, rather than by quinquenniums, it is found that this period begins at 13 years of age and is not coincident in females and in males. Among the former it sets in rather sharply at the age of 12, whereas among the boys the flare up does not manifest itself until the age of 16. This distinction was found to hold good for several large cities, and probably is governed by the onset of puberty. This uniform periodicity in the increase of deaths from tuberculosis, taking place in both girls and boys at a definite year of life, leads to the conclusion that the disease is due to an "auto-genous reinfection" from some latent focus, rather than a fresh infection from a tuberculous individual.

It would seem that the best way to begin to combat this high mortality from tuberculosis would be to establish preventoriums for infants in connection with the large cities. These institutions should be situated in the country about two hours' train ride from the city. They should be built with many balconies, so as to provide for an outdoor life, and should be conducted by children's specialists according to the most approved methods. One or more wetnurses should be provided. The infants should be kept at the institution for at least a year. This central preventorium for infants could well serve as the administrative center for a system of boarding out infants in the farmhouses of the

surrounding country, under supervision of the physician and nurses of the institution; babies who were not thriving could be returned to the precincts of the preventorium for special care and treatment. There is good reason to believe that by this means thousands of babies in the large cities, who will be infected by their parents, could be saved and grow to be healthy. This question is particularly opportune and urgent at the present time, when many soldiers will return to their homes having communicable tuberculosis. The problem of the protection of older children against tuberculosis may likewise be said not to have been considered seriously in the United States.

One measure which the author suggests to guard against the tuberculosis of maturity is the establishment throughout the country of preventoriums similar to that at Farmingdale, N. J. To such institutions should be sent children who are poorly developed and undernourished and who give a positive tuberculin reaction. If it is true that infection at this period of life emanates from a focus within the body, then malnutrition should play a dominant rôle in the selection of the cases. These children should be kept in the country for from three to six months.

From the study of the mortality statistics, Hess concludes that it is inadvisable to make the age of admission from 4 to 14 years, as is done in France, since the high mortality does not begin until 12 years in girls and 16 years in boys. In view of the great need for preventoriums it would seem wise only to accept girls aged from 10 to 16 years and boys aged from 14 to 18 years, in other words, two years before the onset of the high mortality. With this change in the age of admission comes the advisability of providing separate preventoriums for boys and for girls. Finally, it seems possible that some affiliation might be made with agricultural schools, whereby these children could be referred to these institutions and trained in a permanent outdoor occupation.

Louis I. Harris⁵¹ describes the measures carried out by the New York Department of Health to combat tuberculosis among children. The inspection and control of the milk supply by the bureau of foods and drugs from its source to its ultimate point of distribution is not only a preventive of gastro-intestinal diseases, septic sore throats and other infectious diseases, but also of tuberculosis. Pasteurization of milk, now mandatory in New York City, is preventive of tuberculosis among children.

The baby welfare stations, maintained by the department of health for the dietetic and hygienic guidance and supervision of infants, are also of value in the prevention of tuberculosis.

51. Harris, L. I.: What Are We Doing to Prevent Tuberculosis Among Children? *Am. J. Pub. Health* 8:131 (Feb.) 1918.

Parents are taught to give special attention to proper treatment and aftercare for those who suffer from measles and whooping cough, diseases which are notoriously predisposing causes of tuberculosis.

The work of the bureau of child hygiene, which has as one of its chief functions the periodic medical examination of school children, may justly be regarded as the most effective weapon with which the department of health wages its attack against tuberculosis among children. The bureau exercises a constant supervision over 2,000 children, who have been exposed to tuberculosis and whose physical condition makes them susceptible to the disease. The bureau examines children between 14 and 16 years of age, who apply for working papers. This is a means of sifting out those who appear to be susceptible to tuberculosis, as well as those who give evidence of an already existing infection.

The examination of public school teachers in whom tuberculosis is suspected has resulted in the exclusion of a number of actively tuberculous teachers. School lunches are distributed free to ill nourished children. This is valuable chiefly as a palliative measure.

The twenty tuberculosis clinics of the department of health provide a means for the diagnosis, treatment and instruction of children exposed to tuberculosis, and of those susceptible or giving evidence of the disease. The department of health has equipped two ferry boats to care for adults who are unwilling or unable, or who are delayed in entering hospitals, and for exposed and infected children. It has provided for the care in special tuberculosis hospitals of 350 active cases of tuberculosis in children.

Harris thinks the segregation and forcible detention in Riverside Hospital of about 200 patients, who would not observe proper care in the home, has been most helpful, and that such detention deserves more general adoption. It would close one way of transmitting tuberculosis to children and others.

W. D. Beadie⁵² outlines the following as preventive of tuberculosis among children: Prenatal care should be given expectant mothers. Children born of an actively tuberculous mother should be removed to a safe environment immediately after birth, and especially should an actively tuberculous mother be compelled to refrain from nursing her infant. Maids in a household, and those having the care of young children generally, should be examined for tuberculosis. Bovine tubercle bacilli have been found in pulmonary tuberculosis and in disease of the glands and joints. The laws requiring cattle to be tested should be more stringently enforced. Since pasteurized milk has been used more

52. Beadie, W. D.: Prevention of Tuberculosis in Children, *Minnesota Med.* 2:181 (May) 1919.

generally, there has been a marked reduction of this form of infection in children. More work should be done along the lines of school inspection. Education of older children by physicians and health officers would aid greatly in the prevention of tuberculosis.

E. Friedman⁵³ reviews the literature on the frequency, portal of entry, pathology, symptoms, diagnosis and prophylaxis of tuberculosis in infancy and childhood. From his study, he says it is evident that the child must figure prominently in every movement calculated to check the progress of tuberculosis. The fundamental principle in prophylaxis consists in removing a child from a tuberculous environment, particularly during the first three or four years of life. It is at this period that the body defenses are wholly inadequate to cope with tuberculous infection and the toll exacted by death is appalling.

Armand-DeLille⁵⁴ describes the methods, particularly those of the "Oeuvre Grancher," instigated in France to prevent tuberculosis in children. This institution finds homes in the country where children of tuberculous parents can be placed. Children from 3 to 15 years of age are accepted, but no child who is ill or has signs of latent tuberculosis is eligible. The children are first taken to the central office of the organization, where they are fitted out with clothes and operated on for adenoid vegetations if necessary. They are then taken to their destination. A physician makes daily visits, and once a year officers of the society make rounds of inspection. The results have been marvelous; none of the children have become tuberculous. At the age of 13, if the parents are living and desire the children, they are returned to them. Occasionally a child is recalled by the death of the tuberculous parent. At first the society had only twenty-seven patients; before the war the number had increased to 810; at present there are 400 in residence.

C. Ferreira⁵⁵ inaugurated in Brazil a movement for the care of children of tuberculous parents similar to that of Grancher in France. The work was begun in 1908, and in 1916 fifty-eight children, forty-two girls, aged from 2 to 16 years, and sixteen boys, aged 2 to 10 years, were being cared for. At present, the organization has a large sanitarium at Brazanca and is planning two more sanitariums and two preventoriums.

C. Ferreira⁵⁶ finds that tuberculosis causes only 1.2 per thousand of the general mortality of the children of S. Paulo. In fourteen years (1902-1916) there had been recorded 186 deaths from pulmonary.

53. Friedman, E.: Tuberculosis in Infancy and Childhood, *Colorado Med.* **16**:8 (Jan.) 1919.

54. Armand-De Lille, P.: Campaign Against Infantile Tuberculosis in France, *J. A. M. A.* **71**:1 (July 6) 1918.

55. Ferreira, C.: Tuberculosis in Children, *Ann. Paulistas d. Med. e. Cir. S. Paula* **10**:97, 1919.

56. Ferreira, C.: Protection of Children of Tuberculous Parents, *Brazil-med.* **32**:153 (May 18) 1918.

eighty-three from abdominal tuberculosis, and forty-three from tuberculous meningitis, a total of 350 deaths from tuberculosis among children under 10 years of age. During the last few years a vigorous campaign against tuberculosis has still further reduced this mortality rate.

A. F. Hess⁵⁷ reports the results obtained in the preventorium at Farmingdale. During the two years of its existence, thirty-six infants, from 1 month to 1 year of age, were admitted. A number of these weighed less than seven pounds. In all but one instance the mother was tuberculous, and in all but seven instances did the mother's sputum contain tubercle bacilli, so evidently the mother was the most frequent source of infection. During the first few months, infants already infected, as shown by a positive tuberculin reaction, were admitted to the preventorium, but it was found impossible to prevent the rapid development of tuberculosis in them, so later only those giving a negative reaction were received. In all twenty-eight infants, with a negative tuberculin reaction, have been cared for.

Of these, five died, two from diphtheria, one from enteritis, two from marasmus. Hess does not regard these results as being discouraging, and does not hesitate to give the opinion that it is quite possible to save infants of tuberculous mothers. Moreover, he feels it a duty to provide for these infants. At present, they are abandoned to their fate and are only individuals left out of consideration in the tuberculosis propaganda being spread so rapidly through the country.

P. Nobécourt and J. Paraf⁵⁸ call attention to the hospital wards as the source of tuberculous infection in infants, reporting two instances of infants evidently contracting the disease in a hospital creche. The first patient never left the hospital as the mother remained there as a nurse. The child developed well until 11 months old, when she contracted whooping cough; then there was loss of appetite, diarrhea and fever, with dullness, bronchial breathing, and crepitant râles at the base of both lungs. The diagnosis of tuberculosis was confirmed by the roentgenoscope and tuberculin reaction.

The second child developed well until the fifth month, when she showed evidences of a tuberculous bronchopneumonia. The child died two months later and necropsy confirmed the diagnosis.

Hospital infection may be due to direct infection from a nurse or attendant or indirect infection from a contaminated ward. Two tuberculous infants had been in the ward shortly before the children referred to by the authors which emphasizes the importance of disinfection after removing a tuberculous patient.

57. Hess, A. F.: Tuberculosis Preventorium for Infants, *Am. Rev. Tuberc.* **1**:669 (Jan.) 1918.

58. Nobécourt, P., and Paraf, J.: Tuberculosis of Infancy, *Arch. de méd. d. enf.* **22**:355 (July) 1919.

R. M. Smith⁵⁹ discusses the danger to children from tuberculous cattle. He believes that, although bovine tuberculosis represents only a small part of the disease in children, it is very important and can be prevented. It has been estimated that 25 per cent. of all cases of tuberculosis in children under 5 years of age are of bovine origin, and that in New York City from 6 to 10 per cent. of the children who die of tuberculosis each year in the hospitals die of bovine tuberculosis. Smith investigated a series of sixty-seven cases of bone tuberculosis in children, and found that 70 per cent. were of bovine origin. Of the cases in children under 1 year in this group, all were of bovine origin, and under 4 years, 78 per cent. were of bovine origin. Smith says that the real hope of eliminating bovine tuberculosis rests in prevention, not treatment. As infection comes exclusively from milk or milk products, cream, butter, ice cream and cheese, all milk must be pasteurized, unless it is positively known to come from a herd free from tuberculosis. But milk must be pasteurized properly or false standards are established, and physicians should insist on some sort of inspection and supervision of pasteurizing plants.

C. M. Hilliard⁶⁰ found that at least 10 per cent. of the dairy cattle supplying milk to infants, children and adults are infected with tuberculosis. The problem of prophylaxis resolves itself into the elimination of tuberculous cattle or the pasteurization of milk. The author believes that one of the most important functions of the antituberculosis league is to bring about compulsory pasteurization of milk.

E. Maragliano⁶¹ brings to date his report on the vaccination of children and adults against tuberculosis, which he has been advocating for twenty-five years. The method is to introduce dead tubercle bacilli subcutaneously, and he believes that from this focus will be produced antigens which will pass into the circulation and slowly and progressively induce the production of immunizing bodies. He has proved by clinical and biologic tests that antibodies are actually produced. The vaccination was applied from 1907 to 1914 to 3,702 members of families with tuberculosis. The history of 1,893 has been obtained up to 1915. Of this number, 1,819 were living, sixty-three had died from other than tuberculous processes, and only eleven had died from tuberculosis. All persons vaccinated in 1907 were found to be in good health. In twenty-six persons vaccinated earliest, persistence of immune bodies and antibodies was demonstrated. Maragliano believes

59. Smith, R. M.: *Danger of Children from Tuberculosis in Cattle*, Boston M. & S. J. **177**:657 (Nov. 8) 1917.

60. Hilliard, C. M.: *Tuberculosis in Dairy Cattle*, Boston M. & S. J. **177**:654 (Nov. 8) 1917.

61. Maragliano, E.: *Vaccination Against Tuberculosis*, *Riforma med.* **35**:542 (July 5) 1919.

that the only efficient means of prophylaxis against tuberculosis is to acquire a specific resistance against the bacillus, and he feels that his work has opened a practical means to this end.

W. C. Rivers⁶² believes that school attendance is actually responsible for the greater part of juvenile phthisis, and from statistics based on medical literature, and his own experiences, he draws the conclusion that there is much more phthisis among children of school age than among those under this age. He believes that school attendance predisposes to tuberculosis by lowering the general health through the indoor confinement and restraint.

TREATMENT

Meyer-Solis Cohen⁶³ has made a comparative study of the therapeutic effects of various forms of tuberculins, vaccines and serums in pulmonary tuberculosis in children. He reports the results in fifty-one children.

Ten boys and nine girls, from 2½ to 15 years of age, were given Koch's old tuberculin. Seventeen were in the incipient stage of the disease, one was in the moderately advanced stage, and one in the far advanced stage. The initial dose varied from one-billionth to one-millionth of a milligram. The dose was increased in thirteen cases but held in six. It was not decreased in any. The largest dose given was one five thousandth of a milligram. The interval between doses was from three to five days. A favorable reaction followed one or more of the doses in thirteen children; an unfavorable one resulted in sixteen children. In one child no reaction was observed. Benefit from the tuberculin treatment was distinctly noted in thirteen of the children. Six were not benefited by it. None were harmed.

Bacillen emulsion was given to fourteen children. Twelve were in the incipient and two in the moderately advanced stage. The initial dose varied from one-hundred millionth to one millionth of a milligram. The initial dose was increased in every case, the highest being one five hundred thousandth of a milligram. The interval between doses was from three to five days. The tuberculin seemed to be beneficial to nine patients, of no benefit to five and harmful to none.

Tuberculin Ruckstand was administered to thirteen children. Seven were in the incipient stage, four in the moderately advanced stage and one in the far advanced stage. The initial dose varied from one-hun-

62. Rivers, W. C.: Juvenile Consumption and School Attendance, *Brit. J. Child. Dis.* **15**:6 (Jan.-March) 1918.

63. Solis-Cohen, M.: Comparative Study of Therapeutic Effects of Various Forms of Tuberculins, Vaccines and Serums in Pulmonary Tuberculosis in Children, *Arch. Pediat.* **35**:11 (Jan.) 1918.

dred-millionth to one-millionth of a milligram. Twelve patients seemed distinctly benefited during the treatment, one was not benefited, none were harmed.

Six boys and four girls were given bouillon filtrate by mouth. Eight were in the first stage of the disease, one was in the second, and one was in the third stage. The initial dose was from one-hundred-millionth to one millionth of a milligram. Six patients appeared to be distinctly benefited; four seemed unaffected; none seemed harmed.

Eleven children were given two different forms of tuberculin at the same time, seven were benefited, and in four there was no effect. Six children, all in the first stage of the disease, were given Sherman's nonvirulent tubercle bacilli vaccine. The effect was beneficial to one patient, harmful to one, and negative to four.

Seven children were given both Sherman's nonvirulent tubercle bacilli vaccine and Sherman's catarrhal combined vaccine. Six were in the first stage and one was in the second stage of the disease. The general results seemed beneficial in two cases, harmful in one and negative in four.

Six children were given Bruschettini's serum vaccine. One patient seemed benefited, one seemed worse, four seemed unchanged during the treatment. Seventeen of the patients were given at different times several forms of tuberculin, vaccines and serums. None of the combinations of different forms of tuberculin seemed to be of much value.

Cohen thinks it is impossible to draw positive conclusions from the small number of cases studied. But it would seem, that the kind of tuberculin, vaccine and serum used did have some influence on the results obtained. The tuberculins gave better results than the vaccines and serums. Tuberculin Ruckstand to a marked degree and old tuberculin to a slighter degree, properly administered, offer hope of benefiting children with pulmonary tuberculosis. Bacillen emulsion, bouillon filtrate, Bruschettini's serum vaccine and the simultaneous employment of Sherman's non-virulent tubercle bacilli vaccine with Sherman's catarrhal combined vaccine, do not give results to warrant their being recommended. Cohen advises, however, that when one form of tuberculin fails to be of benefit another form may be.

E. Lackner⁶⁴ has had a favorable experience with the tuberculin treatment of tuberculosis in children, but he believes much more work must be done in this direction. He advises an initial dose of 1 1,000 mg. of old tuberculin, gradually increased to 1 c c, which he reaches after from nineteen to twenty injections, given at five-day intervals. As a rule, he observes the patient's temperature for three days before

64. Lackner, E.: Tuberculin Treatment of Tuberculosis in Children, Illinois M. J. 36:76 (Aug.) 1919.

commencing treatment, taking two hourly temperatures during the day and four hourly at night. After the injection of tuberculin, the same procedure is followed. A rise of from 1 to 3 degrees over anything recorded previous to the injection is regarded as a reaction. After the tolerance of the patient is determined, treatment can be continued without a reaction. Lackner is fully convinced that the dose of tuberculin must not be so large as to cause a reaction. It must always be well diluted, in order to prevent focal reactions and reactions at the point of injection, and should be given at five-day intervals. For the length of treatment, Lackner quotes Koch, who gives an average of twelve weeks for pulmonary and bronchial gland tuberculosis; thirty-five weeks for tuberculosis of the pharynx and larynx, seven weeks for tuberculosis of the pleura, ten weeks for tuberculosis of the peritoneum, eleven weeks for tuberculosis of the bones.

Lackner believes that latent forms of tuberculosis are positively helped with tuberculin and the forms occurring between 5 and 10 years are more easily affected than those in the earlier and later periods. Miliary tuberculosis, severe affection of both lungs, and degeneration of the parenchymatous organs are contraindications to the use of tuberculin.

De los Terreros⁶⁵ has treated twelve children with various forms of tuberculosis with Spengler's immune bodies. He gave the treatment a thorough trial for four years. The results were good in six children; fair in three and in three the disease continued a progressive course. Two of the children died. The outcome was better the earlier the stage and the older the child.

R. C. Newton⁶⁶ reports seven cases of tuberculosis in children treated with tuberculin, which he thinks illustrate several important truths in tuberculin treatment, namely: the frequent unexpected benefit of small doses of the drug; the great importance of having the patients under treatment at the earliest possible moment, the necessity of at times changing the form and dosage of the tuberculin; the desirability of using vaccines and different agents, in conjunction with the tuberculin, the importance of every available hygienic measure; the treatment of children in the pretuberculous stage.

The author's cases include four cases of tuberculous peritonitis and three of pulmonary tuberculosis. Of the four cases of peritonitis, three patients were brought under treatment within a few weeks of the appearance of the ascites and the improvement was prompt and gratifying. The fourth patient took much longer to recover. The

65. de los Terreros, C. S.: Spengler's Immune Bodies in the Treatment of Tuberculosis in Children, *Arch. españ. de pediat.* **3**:263 (May) 1919.

66. Newton, R. C.: Tuberculin Therapy in Children, *Med. Rec.* **96**:459 (Sept. 13) 1919.

three patients with pulmonary tuberculosis also improved under treatment. The author mentions excellent results in three other patients with pulmonary tuberculosis, who came under his care within a few months of the beginning of active lesions. He emphasizes the importance of early treatment, in order to obtain permanent benefit.

J. P. Garrahan⁶⁷ reports his experience with the intradermic injections of tuberculin for diagnosis and treatment in 653 children from 2 to 16 years old. As a diagnostic test he found it more reliable than the von Pirquet test, especially in instances of latent tuberculosis. When suspicious of hypersensitiveness, he advises giving a dose of 0.00001 gm., instead of the usual 0.0001 gm. A positive reaction in an infant is an almost unmistakable sign of active tuberculosis and a repeated negative reaction in older children certainly excludes tuberculosis. According to Garrahan's opinion, treatment with intradermal injections of tuberculin is absolutely harmless, and there does not seem to be any contraindication to its use. He does not, however, share Combe and Jeanneret's optimism as to its efficacy. He advises it as an adjuvant or when climatic and hygienic treatment is not available.

R. Hertz,⁶⁸ who has charge of a sea coast sanatorium for children in Denmark, has given heliotherapy a very prominent place in the treatment of tuberculous disease of the bones and joints. The sun baths are taken for about six hours a day and the children recline or play or stroll about in the open air unclothed. In stormy weather they remain indoors in a large hall built like a green house. The reflection from the water of the bay enhances the effect of the sunlight. The children seem to bear low temperatures better when they are well tanned.

Hertz's results nearly equal those obtained by Rollier at Leysin and he asserts that the cure has been permanent in a much larger number of cases than with the best surgical procedures.

R. C. Newton and S. A. Twinch⁶⁹ compare the results in fifty cases of tuberculosis, mainly osseous and glandular, treated with tuberculin. With a few exceptions, these patients were children, inmates of a home for crippled children, and patients in a hospital clinic. Without tuberculin, 16 recovered, or 32 per cent.; 25 died, or 50 per cent.; 9 are still wearing braces and are under treatment, or 18 per cent. With tuberculin, 33 recovered, or 66 per cent.; 5 were much improved, or

67. Garrahan, J. P.: *Treatment of Tuberculosis in Children*, Prensa med. Argentina **6**:35, 1919.

68. Hertz, R.: *Conservative Treatment of Surgical Tuberculosis*, Ugesk. f. Lager **80**:196, 1918.

69. Newton, R. C., and Twinch, S. A.: *Fifty Cases of Tuberculosis, Mainly Osseous and Glandular, Treated with Tuberculin, Contrasted with Fifty Cases Treated without Tuberculin*, Med. Rec. **94**:407 (Sept. 7) 1918.

10 per cent.; 6 died, or 12 per cent.; 5 are still under treatment, or 10 per cent.; 1 discontinued treatment, or 2 per cent. Of the 16 patients cured without tuberculin the average period of treatment for each case was five years and three months. Of the 33 cures with tuberculin, the average period of treatment for each case was eleven and one-half months. Of the 25 deaths without tuberculin the whole period of treatment was seventy-two years, eleven months, nine days, or three years and fourteen days for each patient. Of the 6 deaths among those treated with tuberculin the total period of treatment was four years, nine months and twenty-nine days, or an average of nine months and thirteen days for each patient. Of those treated without tuberculin, 9 are still under treatment. Of those treated with tuberculin, 5 are still under treatment.

E. Stolkind⁷⁰ discusses the treatment of pulmonary tuberculosis by means of artificial pneumothorax. He says the ideal case is one of advanced pulmonary tuberculosis in one lung, with the other lung at least, clinically normal. The treatment, however, is still indicated, if the disease in the other lung is inactive, chronic or quiescent. Artificial pneumothorax is useful also in acute unilateral pulmonary tuberculous pneumonia, in cases of pulmonary tuberculosis with pleural effusion, spontaneous pneumothorax, or seropyopneumothorax. In the latter instances, the fluid is gradually removed and the gas is introduced. The treatment is indicated also in cases of pulmonary abscess.

Pneumothorax treatment is contraindicated in cases of pulmonary tuberculosis, complicated by other severe diseases. Asthma, too, is a contraindication.

In the treatment with pneumothorax the same complications may occur in children as in adults. The most frequent complications are subcutaneous emphysema and pleural effusion. Subcutaneous emphysema occurs in the great majority of the cases. Usually, it is not extensive, is harmless, and disappears in a few days. More serious is the occurrence of deep emphysema, in which the gas burrows between the endothoracic fascia and parietal pleura or under the visceral pleura. Pleurisy with effusion is the other complication frequently observed. Suppurative effusion, pleural shock, pleural reflex and gas embolism are the most dangerous complications, but occur rarely.

Stolkind believes that the results of treatment with pneumothorax in subacute cases are very satisfactory. Generally, the temperature falls, the cough and sputum lessen, and the tubercle bacilli diminish or disappear. Children and adolescents usually gain weight. The author

70. Stolkind, E.: Treatment of Pulmonary Tuberculosis in Children with Artificial Pneumothorax, *Brit. J. Child. Dis.* **16**:18 (Jan.-March) 1919.

is of the opinion that pneumothorax treatment should be applied in every case of advanced pulmonary tuberculosis, not only in adults, but also in children.

E. Stolkind's advice as to the use of pneumothorax is dangerous, to say the least. Even if the disease is apparently limited to one lung, there is no guarantee that a small hidden focus in the other lung would not light up under the additional strain and cause either a widespread tuberculous bronchopneumonia or a miliary tuberculosis. If the disease in the other lung is chronic or quiescent, there is little doubt but that these catastrophes would occur.

M. H. Beiz⁷¹ reports three cases of the ascitic form of tuberculous peritonitis treated with autotherapy. The first patient was a boy, 5 years old, who had been ill two months with nausea, vomiting, pain in the abdomen and fever. On entrance to the hospital there were signs of tuberculosis at the base of the right lung and a greatly enlarged abdomen. Fifty cubic centimeters of fluid were withdrawn, and 10 c c were injected into the muscles of the thigh. The injection was well tolerated and was followed by a polyuria. The abdomen gradually diminished in size and the ascites disappeared.

The second patient was a boy 11 years old, with a tuberculous ascites. Ten cubic centimeters of fluid was injected beneath the skin of the thigh, and one week later 20 c c were injected. Three other injections of 30 c c were administered at eight day intervals. Little improvement followed and resort was made to heliotherapy with good results.

The third patient was a boy, 10 years old. The first injection consisted of 15 c c. of fluid, which was followed in eight days by another injection. No results followed the injection.

In a fourth patient autotherapy did not give any better results, and from his experience the author does not advise its use. Moreover, he has shown that rest, compression and fresh air are usually sufficient to effect a cure of this form of tuberculous peritonitis.

Ramond and Francois⁷² emphasize that tuberculosis is essentially curable, especially when it involves serous membranes. Their experience with injections of air during the last two years seems to suggest that this method will become valuable in the treatment of tuberculous meningitis. The procedure seems absolutely harmless with the following technic: The lumbar puncture is made with the patient in the reclining position, and about 40 c c. of fluid is withdrawn. The air is

71. Beiz, M. H.: Autoserotherapy in Ascites of Tuberculous Peritonitis. Abstr., *Arch. de méd. d. enf.* **22**:99, 1919.

72. Ramond, F., and Francois: Treatment of Tuberculous Meningitis by Injections of Air Into the Spinal Canal. *Bull. et mem. Soc. med. d. hop.* **41**:1058, 1917.

drawn into a Roux syringe through a long, red hot platinum needle, which sterilizes and warms it. It is then injected slowly through the puncture needle, which has been left in place. The amount of air injected should not exceed one-half or two-thirds of the amount of fluid withdrawn. The injection should be repeated on five or six consecutive days, but no longer, as the nitrogen of the air is not readily absorbed. If oxygen is used, the injections can be kept up indefinitely. The authors' results with this form of treatment have been encouraging.

Bausa⁷³ deplors that he has never been able to save a child with tuberculous meningitis. He suggests several procedures in the treatment of this condition. The withdrawal of large amounts of spinal fluid, a method not dangerous, as cerebrospinal fluid forms rapidly; a canula might be left in the spinal canal to insure permanent drainage and to enable an antiseptic to be applied directly to the meninges. Heliotherapy, local heat and antiserums might be used as adjuvants. Bausa believes that tuberculin might be of value during the prodromal stage.

William Aston⁷⁴ lays stress on the frequent examination of all delicate children under school age, and especially those with a tuberculous family history. He considers it a duty of utmost importance for all public authorities to see that sufficient attention is paid to the prevention and treatment of tuberculosis among children. A campaign should be carried out to establish convalescent camps in the country, open air schools and day sanatoriums for the early cases, and to provide proper institutional care for the reception of all children in whom the disease is definitely established.

V. Y. Bowditch⁷⁵ describes the children's pavilion at the Sharon Sanitarium. It is intended to be a combined sanatorium and school for debilitated children with suspected tuberculosis, and for children in the earliest stages of pulmonary and glandular tuberculosis. Children of parents of moderate incomes have preference in being admitted.

4744 Prairie Avenue.

73. Bausa, J. M.: Treatment of Tuberculous Meningitis, *Am. Rev. Tuberc.* **3**:51, 1919.

74. Aston, W.: The Care of Tuberculous Children, *Brit. J. Tuberc.* **13**:124 (July) 1919.

75. Bowditch, V. Y.: Children's Pavilion at the Sharon Sanitarium, Boston M. & S. J. **178**:553, 1918.

American Journal of Diseases of Children

Vol. 19

MAY, 1920

No. 5

SCORBUTIC BEADING OF THE RIBS

ALFRED F. HESS, M.D., AND LESTER J. UNGER, M.D.

NEW YORK

For many years beading of the ribs has been regarded as a sign characteristic of rickets. The "rachitic rosary" is sought for in order to establish the diagnosis, and its presence is considered pathognomonic of this disorder. In the course of a study of rickets begun about two years ago, we became especially interested in this sign, which was found to be one of the most valuable in following the course of this disease. It was soon appreciated that it varied greatly not only in degree, but also in kind, and that in order to make reliable use of this sign several factors always must be taken into consideration. As is well known, beading may be very slight, or the costochondral junctions may stand out, so as to be evident to even the casual observer. The clinical importance of this slight degree of beading, found so frequently on careful examination, is as yet undetermined. In order to follow the variations in the beading, six grades were formulated, which were designated in the records by plus minus (\pm) or plus (+) signs, + + + representing the maximal degree. It may seem that an empirical method of this kind is too inexact to furnish reliable clinical data. An experience of several hundred cases and more than one thousand examinations, has demonstrated, however, that with even moderate experience one can obtain surprisingly uniform results by this means. It has almost never happened that the physicians of the clinic differed in their appraisal of the beading to the extent of more than one degree; in other words, one observer might rate the beading at plus minus (\pm) and another at one plus (+), but the difference of opinion was not greater. A large number of infants were followed in this way; the examinations were made every month by one of us (A. F. H.), and a careful record was kept of the beading and other signs generally associated with rickets.

As stated, beading differs not only in degree, but also in character. The costochondral junctions as a rule are rounded, smooth, knobby. There may be, however, what we have termed "angular beading," the junction taking on a steplike form, as if the abutting ends of the cartilage and of the bone were of unequal size, and not well fitted to each other. At necropsy such is found frequently to be the case; the cartilage overtops the bone so that on palpating the joint there is a precipitous fall as we run the finger outward from the surface of the

cartilage to that of the bone, or a sudden elevation on palpating the rib from without inward toward the sternum.¹ This angular beading is met with more often in infants more than 1 or 1½ years of age, and in many cases should be regarded as "residual beading," remaining after the rachitic process is no longer active. Cases which show residual beading are, therefore, not appropriate to test the value of therapeutic agents. In these instances cod liver oil will generally fail to diminish the beading, even though it be of rachitic origin.

In the course of rickets, as is well known, the lower free border of the ribs may gradually become everted and project forward. There may occur what has been termed "flanging of the ribs." Flanging also takes place usually in the later stages of the disorder, when it shows a tendency to become stationary or to recede. This change in the bony structure naturally affects the beading, sometimes obliterating it, and in other instances causing it to become less evident externally. Wherever this eversion occurs, all attempts at following the course of the beading, and the progress of the disorder which gives rise to it, must be abandoned, and the case considered unsuitable for further study from this viewpoint.

As observed by many investigators, the beading of the ribs occurs most often in the middle tier, especially in the fifth, sixth and seventh ribs, and less often in the upper and in the floating ribs. Why such is the case is not thoroughly understood. Its explanation is involved in an understanding of the pathogenesis of beading. Some have thought it due to the fact that these ribs grow most rapidly, and others that there is a greater degree of motility in the costochondral junctions at this level. A clinical test of the latter hypothesis proved inconclusive. In several cases we attempted to immobilize one half of the thorax by applying strips of adhesive plaster to the chest from the sternum to the spine. These were applied continuously for about two months, but did not reduce the rosary. On the other hand, in another group of cases the costochondral junctions were subjected to vibration daily, for ten minutes, during the same period of time, without having a decided effect in either an increase or a diminution of the size of the junctions.

We do not wish, however, to discuss beading of the ribs from the point of view of rickets, but rather to draw attention in some detail

1. Probably it is this condition which Barlow refers to in his article on Scurvy (*Cyclopedia of the Diseases of Children*, 1890, Philadelphia 2:272): "What had been taken during life for beads proved to be simply the ends of the costal cartilages abutting against ribs which were so extremely wasted that their anterior ends by no means came into complete apposition with the whole of the ends of the costal cartilages. There were no beads at the posterior surface. It was a wonder that the ribs had not separated from the costal cartilages or fractured beyond, they were so exceedingly brittle. There was, in fact, nothing but a shell of bone containing a little soft red medulla. On the parietal pleura of both sides there were numerous petechiae corresponding with the ribs."

to a fact which we recently pointed out,² namely, that beading may be due to causes other than rickets, and more especially that there is true *scorbutic beading*.

The difficulty of concluding in a case of scurvy that the beading is scorbutic is that possibly complicating rachitic beading may likewise be present. We have had exceptional opportunity, however, to see cases where this explanation could not well be advanced, where beading developed in spite of the fact that infants had been receiving adequate amounts of cod liver oil for long periods. In three instances, not only marked beading, but enlargement of the epiphyses as well, developed, although the babies had been given cod liver oil, three teaspoonfuls daily, for a preceding period of four months or more. This treatment had been begun when the babies were only 2 or 3 months of age. Further proof of the scorbutic character of these lesions was the fact that both the beading and the enlarged epiphyses were reduced markedly in size (Table 1) within six weeks after giving orange juice, three teaspoonfuls daily. Table 2 illustrates the fact that where cod liver oil has not been taken, rachitic beading may develop in the course of scurvy and persist in spite of many months of antiscorbutic treatment.

TABLE 1.—SCORBUTIC BEADING IN TWO CASES OF SCURVY (N. M. AND I. L.)

This sign developed in spite of a dietary that included cod liver oil, and decreased rapidly when orange juice (15 c.c. daily) was added.*

Age, Months	Beading	Epiphysis	Age, Months	Beading	Epiphysis	Diet
2	++	++	6	-	-	Cod liver oil (15 gm. daily)
6	+++	++	7	++	+	Orange juice added
7	+±	+	8	±	±	(15 c.c. daily)
9	+	+	9	±	±	

* ± signifies the least, and +++ the maximum degree of beading.

Another group of cases significant in this connection is composed of infants who have scurvy, and who on receiving an antiscorbutic—one tablespoonful of orange juice or two tablespoonfuls of canned tomato—lost the beading of the ribs as well as the signs typical of scurvy. This also is illustrated in Table 1, and by other cases which we have observed. There can be no question of having cured rickets instead of scurvy by means of this orange juice and tomato. An experience of a year ago with a larger number of infants who were found to be suffering from acute or from latent scurvy was striking in this regard. The beading, which was of most marked degree, melted away under the influence of treatment with canned tomato. In passing, it may be suggested that this involvement of the costochondral junctions is the cause of the thoracic tenderness which is so evident when scorbutic infants are grasped by the thorax.

2. Hess, A. F., and Unger, I. J.: J. A. M. A. **24**:217 (Jan.) 1920.

Tobler's³ experience in a recent epidemic of scurvy in Vienna is illuminating in this particular as it concerns older children, between the ages of 2 and 15 years, who are far less subject to rickets. In more than 200 cases he noted the development of a rosary almost regularly. Tobler was uncertain, however, whether the swellings should be attributed to scurvy or whether they were entirely of rachitic origin.

In connection with this subject, a case described many years ago by Fraenkel⁴ is convincing. A child, 7 years of age, developed acute scurvy. The thoracic beading was found clinically and was verified at the necropsy; its true scorbutic character was substantiated by microscopic examination. This would seem to constitute conclusive evidence of scorbutic beading from the pathologic standpoint.

TABLE 2.—RACHITIC BEADING IN A CASE OF SCURVY (S. A., AGED 15 MONTHS)

Cod liver oil had not been included in the dietary. Beading was not diminished by an antiscorbutic, although all the scorbutic signs disappeared.

	Rosary	Epiphysis	Diet
1917			
April.....	+++	++	Malt soup
June.....	++	+	Canned tomato, 15-30 c.c. added
July.....	++	+	Canned tomato, 45 c.c.
August.....	++	++	
September.....	+++	++	
October.....	+++	+++	Canned tomato, 120 c.c.
November.....	++	++	
December.....	++±	++±	
1918			
January.....	++±	++±	
February.....	++±	++±	
March.....	++±	++±	

There can be no question that scorbutic beading occurs in animals. This change has been noted by many who have produced experimental scurvy. It is one of the most vivid and striking phenomena on opening the thorax of the scorbutic guinea-pig, and is the counterpart of what is found in infants. Frequently, it is most marked on the pleural aspect, it involves the middle tier of ribs, and is the site of subperiosteal hemorrhage. It can even be differentiated into an angular and a round variety. Although this alteration at the costochondral junctions has been observed frequently, it has, to our knowledge, not been brought forward as essentially scorbutic in nature. Some observers have passed it by with mere mention, others have termed it "pseudo-rachitic," whereas still others, notably Holst and Froelich,⁵ although showing its value in the study of guinea-pig scurvy, have not attempted to correlate it with the symptomatology of human scurvy. These authors showed that the microscopic lesions at the costochondral junctions are typical of scurvy—the zone of bone disintegration, the framework

3. Tobler, W.: *Ztschr. f. Kinderh.* **18**:63, 1918.

4. Fraenkel, E.: *Fortschr. a. d. Geb. d. Roentgenstrahlen*, Supplement 18, 1908.

5. Holst, A., and Froelich, J.: *Ztschr. f. Hyg. u. Infektionskrankh.* **72**:1, 1912.

marrow, the subperiosteal and medullary hemorrhages, are all present. The experience of others, as well as our own, serves merely to bear out their conclusions. It may be stated, therefore, that clinical signs of beading can be made out distinctly in guinea-pigs during life, that it is evident on gross examination after death, and that microscopic examination serves to verify its scorbutic nature. The work of Hart and Lessing on monkeys is corroborative in this respect; they described enlargement of the costochondral junctions which they term a "rachitic rosary," in spite of the fact that they found on microscopic examination lesions typical of scurvy.

In connection with the subject of beading, the recent work of Aschoff and Koch⁶ is of interest. In their pathologic studies on scurvy among soldiers they frequently describe beading of the ribs, which they attribute to an infraction of the costochondral junctions. A convincing account of scorbutic beading is contained in an article by Boerich, which describes scurvy in Russian soldiers. He mentions the beading of the ribs, especially from the third to the seventh, which led, in many cases, to a diagnosis of pleurisy or pneumonia by the army surgeon. In adults the phenomenon can hardly be attributed to rickets.

Beading is as characteristic a sign of infantile scurvy as it is of rickets—appearing and disappearing with the other signs and symptoms of the disorder. As mentioned in the article referred to above, it occurs also in connection with beriberi, another so-called deficiency disease. Andrews⁷ reported that among eighteen necropsies made on infants dying of beriberi, he encountered three cases with beading of the ribs; in a personal communication he has stated that these were the only instances of "rickets" which he met with at necropsy in the Philippines. We have found that in some instances beading disappeared on adding 30 c.c. of autolyzed yeast to the diet. It is of interest to learn that beading occurs in association with pellagra. Weston⁸ makes this observation in his article on pellagra in children, and Agostini⁹ states that "up to 19 years of age, one-fourth of these unfortunates show rickets." It is probable that in mentioning these causes of beading we have not exhausted the possibilities from an etiologic standpoint.

It will be remembered, that until Barlow's writing, scurvy was confused with rickets, that even Moeller, who was one of the first to sense the distinction between the two clinical conditions, considered infantile scurvy to be merely "acute rickets." For many years a lively discussion followed as to whether the so-called Barlow's disease was not merely a form of rickets. Hirschsprung contended stoutly for this

6. Aschoff, L., and Koch, W.: *Skorbut*. Gustav Fischer, Jena, 1919.

7. Andrews, V. L.: *Philippine J. Sc.* **7**: Sec. B, 67, 1912.

8. Weston, W.: *Am. J. Dis. Child.* **7**:124 (Feb.) 1914.

9. Harris, H. F.: *Pellagra*. Macmillan Co., New York, 1919.

point of view, and many pathologists, for example Nauwerck, regarded the scurvy merely as "an episode in the course of rickets."¹⁰ Others believed that infantile scurvy developed necessarily on a rachitic basis. In England, Cheadle held this view. The fundamental basis for this protracted confusion between the two disorders was the fact that beading of the ribs was to be found in almost all cases of scurvy, and this sign was looked on as characteristic solely of rickets. There could be little misinterpretation of the other clinical signs and symptoms—the skin hemorrhages, the subperiosteal swelling, the marked tenderness and pain resembled in no respect the signs and symptoms of rickets. When we read in the excellent investigation of infantile scurvy carried out some years ago by the American Pediatric Society,¹¹ that 152 of the 340 cases analyzed showed symptoms of rickets, the question arises as to whether the diagnosis of rickets was not in many cases based on the presence of beading.

It is evident, therefore, that the fact that beading of the ribs may be likewise of scorbutic origin has clinical and diagnostic significance. Unless we are certain that a baby has received an adequate quantity of antiscorbutic food, we are not justified in considering the enlargement of the costochondral junctions of rachitic origin. The rosary may, indeed, be of twofold nature, as these two nutritional disorders may, and frequently do, exist concomitantly. This does not imply, however, that "very possibly the same defect in diet which produced the one produced the other also," for we know that a small quantity of the fruit juices will prevent scurvy, but not rickets, and, on the other hand, that cod liver oil will generally prevent the development of rickets, but has no prophylactic value for scurvy.

CONCLUSIONS

Beading of the ribs, the so-called rachitic rosary, should not be regarded as pathognomonic of rickets. It occurs very frequently in connection with infantile scurvy and is one of the typical signs of this disorder, developing in the course of the disease, and disappearing rapidly with the recession of the other symptoms when an antiscorbutic foodstuff is given. This view is borne out by clinical observations on man and on animals, as well as by postmortem examinations.

The rigid conception of this phenomenon as attributable solely to rickets led to a confusion of infantile scurvy and rickets in the past, and today is responsible for the misinterpretation of many cases of latent scurvy.

10. Schoedel, J., and Nauwerck, C.: Untersuchungen über die Moeller-Barlowsche Krankheit, Gustav Fischer, Jena, 1900.

11. American Pediatric Society Investigation: Arch. Pediat. **15**:481, 1898.

WATER RETENTION IN PNEUMONIA *

HERBERT O. LUSSKY, B.S., M.D.

AND

HUGO FRIEDSTEIN, B.S., M.D.

CHICAGO

It has been the custom at the Children's Memorial Hospital to keep daily weight records of all children under 2 years of age, if not suffering with a contagious disease. Dr. Amberg called our attention to the fact that children who keep up their weight or gaining weight during a febrile disease, may begin to lose weight with the disappearance of the fever. In some cases, this happened abruptly, in others gradually. A closer survey of the cases showed that the loss was more likely to occur in cases of lobar pneumonia. From the years 1914 to 1919 we were able to collect fifty-two cases of pneumonia suitable for our study. In all but one of the twenty-eight cases ending with a crisis, there was some loss of weight coincident with the crisis. This loss was frequently quite marked. The cases are recorded in Table 1. They represent uncomplicated cases. The table gives the age of the children, the duration of the disease before their entrance into the hospital, and the duration of the fever at the hospital. The loss of weight is recorded and the time during which it occurred. Figures 1 and 2 illustrate these conditions very well. In Figure 1 is recorded a loss of one pound; in Figure 2 is recorded a loss of 1 pound and 2 ounces within two days. The average loss of weight of the uncomplicated cases occurring within twenty-four hours, was $9\frac{3}{5}$ ounces. The maximum loss in one day occurred in Case 41—11 $\frac{1}{4}$ pounds; the minimum, with the exception of Case 51 which was without loss, occurred in Case 2—6 ounces in two days.

We were unable to find any relationship between the degree and the rapidity of the loss to either the height of the temperature, as registered during the stay in the hospital, or to the duration of the fever. Neither was there a relationship between the range of the drop in temperature and the loss of weight. Unfortunately, in many instances, the data about the extent of the lung involvement are not sufficiently explicit; so we cannot say anything about a possible relationship between the amount of exudate and loss of weight. Figure 3 is of special interest. The child was brought in the day it was taken sick. On the third day

* From the Otho S. A. Sprague Memorial Institute Laboratory of the Children's Memorial Hospital.

* Read before the Central States Pediatric Society, Oct. 25, 1919.

of the disease an increase in weight began, lasting to the crisis on the seventh day. At this time, the weight dropped a little (about 4 ounces) and remained stationary. With an abrupt increase in weight, an edema of the eyelids and feet became manifest. This disappeared as rapidly as it had appeared. At the same time, the weight fell markedly.

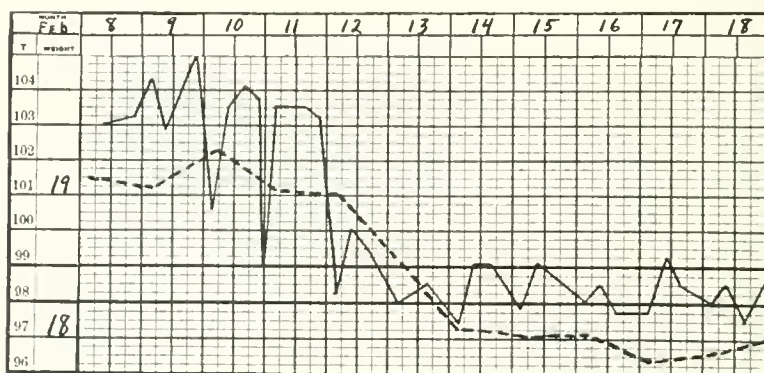


Figure 1

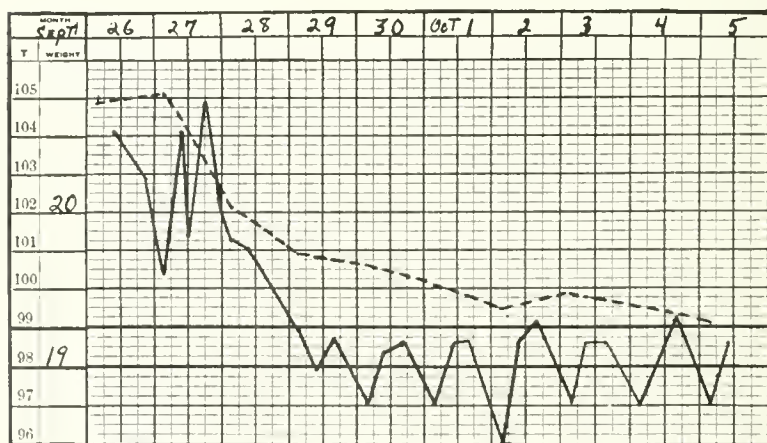


Figure 2

In Table 2 are recorded twenty-two cases of pneumonia which did not end in crisis. Twenty-one of the patients had some complication. In five, there was no loss of weight with the gradual defervescence, and when there was a loss of weight it never was abrupt, but extended over a considerable number of days.

Case 52 is the only uncomplicated case of lobar pneumonia with lysis. It presented a weight curve (Fig. 4) perhaps more in keeping

TABLE 1.—ANALYSIS OF TWENTY-NINE CASES OF PNEUMONIA

Case Number	Age, Months	Duration of Disease before Entrance, Days	Duration of Temperature in Hospital, Days	Definite Crisis	Complication	Loss of Weight	Time of Loss of Weight, Days
2	10	?	2	Yes	None	Ounces 6	2
4	7	1	1	Yes	None	12	3
9	7	7	8	Yes	None	Pounds $1\frac{1}{2}$	3
11	4	4	4	Yes	None	1	2
15	18	4	12	Yes	None	$2\frac{1}{2}$	4
16	19	12	4	Yes	None	1	2
17	12	3	4	Yes	None	$1\frac{1}{2}$	3
19	14	1	3	Yes	None	$1\frac{1}{2}$	3
20	14	8	3	Yes	None	$3\frac{1}{2}$	4
21	16	2	4	Yes	None	$\frac{3}{4}$	2
26	16	8	1	Yes	None	1	1
27	8	5	2	Yes	None	$2\frac{1}{2}$	3
28	12	14	3	Yes	None	2	3
29	13	3	3	Yes	None	1	3
32	6	3	3	Yes	None	$\frac{3}{4}$	1
33	14	4	4	Yes	None	$1\frac{1}{4}$	2
37	14	4	6	Yes	None	$1\frac{1}{2}$	2
38	8	2	6	Yes	None	1	1
40	3	3	3	Yes	None	$\frac{3}{4}$	1
41	11	?	1	Yes	None	$1\frac{1}{4}$	1
42	12	3	5	Yes	None	$1\frac{1}{2}$	2
43	18	3	5	Yes	None	3	2
45	9	6	5	Yes	None	1	1
46	14	3	5	Yes	None	1	1
47	5	3	6	Yes	None	1	1
48	11	4	3	Yes	None	1	1
50	10	3	3	Yes	None	1	1
51	11	4	3	Yes	None	1	2
52	11	8	8	None	None	Increase $1\frac{1}{4}$	12

TABLE 2

Case Number	Age, Months	Duration of Disease before Entrance	Duration of Temperature in Hospital	Definite Crisis	Complication	Loss of Weight, Pounds	Time of Loss of Weight
1	7	5 days	3 days	No	Otitis media	None	
3	10	4 days	7 days	No	Otitis media	None	
5	12	10 days	13 days	No	Enteritis	$3\frac{1}{2}$	Gradual
6	3	7 days	9 days	No	Otitis media	$1\frac{1}{4}$	Gradual
7	11	6 days	3 days	No	None	1	Gradual
8	10	6 days	3 days	No	Otitis media	3	Gradual
10	16	?	5 days	No	Otitis media	None	
12	6	3 weeks	8 days	No	Otitis media	None	
13	12	4 days	3 days	No	Otitis media	None	
14	23	3 days	7 days	No	Meningitis	3	Gradual
18	9	3 days	6 days	No	Otitis media	$1\frac{1}{2}$	Gradual
22	19	2 days	8 days	No	Otitis media	$1\frac{1}{4}$	Gradual
23	8	3 days	6 days	No	Otitis media	1	Gradual
24	11	1 day	7 days	No	Otitis media	1	Gradual
25	13	8 days	9 days	No	Otitis media	$\frac{3}{4}$	Gradual
30	13	6 days	3 days	No	Otitis media	1	Gradual
31	10	3 days	6 days	No	Otitis media	$1\frac{1}{2}$	Gradual
34	2	4 days	4 days	No	Otitis media	$\frac{1}{2}$	Gradual
36	14	4 days	4 days	No	Otitis media	1	Gradual
39	12	6 days	6 days	No	Otitis media	$1\frac{1}{2}$	Gradual
44	10	3 days	8 days	No	Empyema	$2\frac{1}{2}$	Gradual
49	18	7 days	4 days	No	Otitis media	2	Gradual

with what one would expect in a febrile disease associated with an increased metabolism. Here the drop in weight begins at the height of the fever before defervescence begins and proceeds rather uniformly.

Since the most frequent complication in our cases of pneumonia was otitis media, we were anxious to compare these cases with uncomplicated cases of otitis media. We were able to collect the data of eleven such cases, the ages of the patients varying from 4 to 13

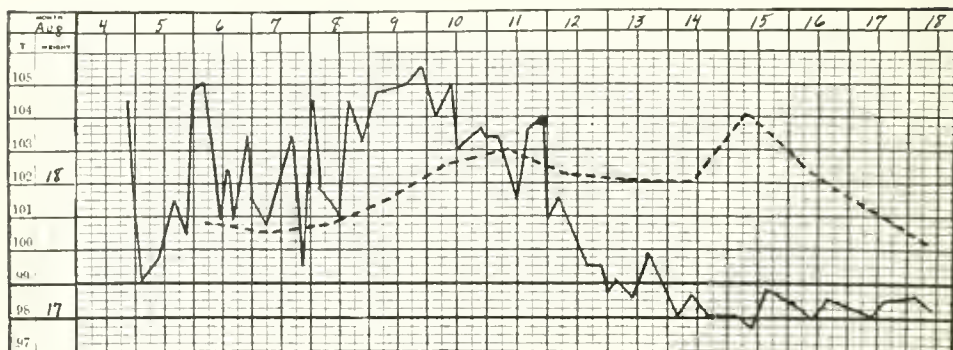


Figure 3

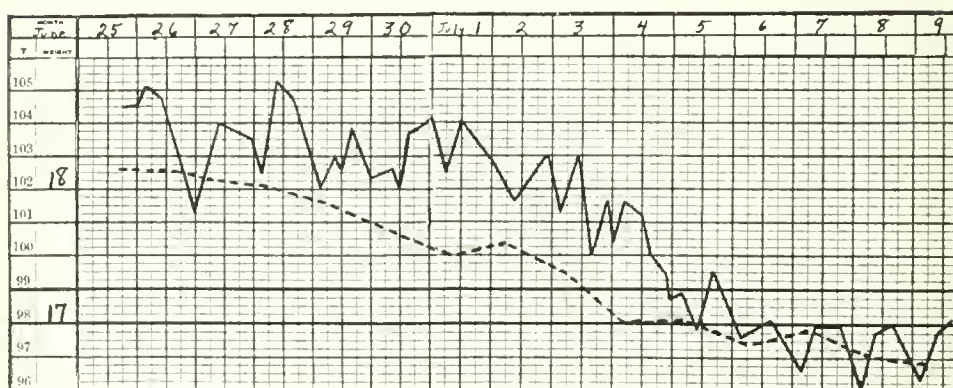


Figure 4

months. In nine of these cases (only one without paracentesis), the fall of the temperature was as abrupt or nearly as abrupt as in the case charted in Figure 5. In three of these cases there was a more or less marked drop of weight associated with the drop in temperature. In one instance, the weight dropped from 17 to 16 pounds and 2 ounces (a loss of 14 ounces); in another from 16 pounds and 9 ounces to 16 pounds and 1 ounce (a loss of 8 ounces) within twenty-four hours, and in a third case 8 ounces were lost from 13 pounds within two days. In

one case there was no loss of weight; in five cases the loss of weight, incidental to the drop of temperature, did not amount to more than 3 ounces. In two of these cases the temperature dropped very considerably, once from 104 to 98 F., and another time from 104 to 99 F. In two cases the temperature dropped more gradually, and in each case there was some loss of weight extending over several days, the loss, however, not being very marked.

The number of our observations is rather small; however, they indicate that cases of lobar pneumonia with crisis are more likely to be accompanied by a marked loss of weight coincident with or rather shortly preceding defervescence. In complicated cases, the weight curve dropped from the beginning of the observation with or without an acceleration of the drop during defervescence. Uncomplicated cases

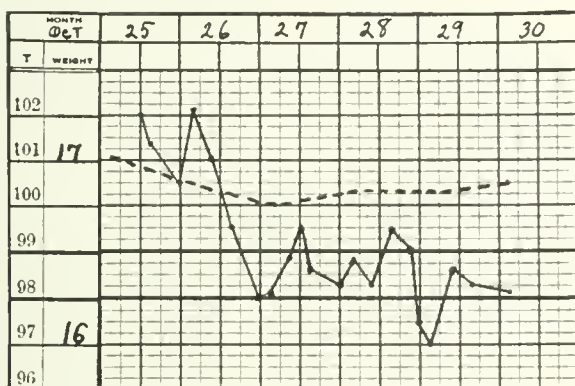


Figure 5

of otitis media may show a rather abrupt loss of weight with defervescence, but this seems to be more the exception than the rule.

Several factors may enter in this abrupt loss of weight in cases of pneumonia. It must be taken into consideration that a considerable amount of inflammatory exudate exists with this disease. Its rapid resolution has been shown to be associated with an increase in the amount of urine as well as in the amounts of the excreted chlorids and nitrogen, as shown by Cook.¹ The absorption and excretion of the inflammatory exudate or of its products may take part in this loss of weight. But this may not tell the whole story. Indeed, the occurrence of such abrupt losses of weight in some cases of otitis media shows that the resorption of the exudate cannot be the only factor concerned. Part, or even most, of this loss of weight may be due to an elimination

1. Cook, H. W.: Nitrogen Excretion in Pneumonia and Its Relation to Resolution, Bull. Johns Hopkins Hosp. **13**:307, 1902.

of previously retained water. Koeppe,² who observed an increase of weight of infants free from nutritional disorders during various febrile attacks, attributed this increase to retention of water.

That there is a marked change in the water economy of the body in pneumonia, as in other fevers, has been accepted by various authors. For instance, Fischer³ states: "Edema is not an uncommon accompaniment of fever. In some fevers it constitutes a symptom so marked that it is looked for clinically; in others, the increased amount of water held by the patient is clearly indicated by his increase in weight and his failure to excrete an amount of water through kidneys, lungs, skin and bowel, the equivalent of that ingested. With remission or discontinuance of the fever there has been noticed by the most careful observers an increase in the output of water by all the water excreting organs above the amount ingested." Woodyatt⁴ and his co-workers put it thus: "Everyone is familiar with the remarkable emptying out of water via the kidneys and skin which may follow the crisis in a case of pneumonia. Liters of water may thus be liberated in a few hours, giving visible proof of the water retention of the febrile stage."

In the case of pneumonia in children we may recall the fact that Maver and Schwartz⁵ were able to demonstrate by means of the Schade elastometer, the presence of edema of the skin which could not be detected by simple palpation. Indeed, changes in the water distribution have been made responsible for the fever occurring under various conditions. The pediatrician is familiar with that conception, particularly through the contributions of Heim and John,⁶ and of Peteri.⁷ Woodyatt and his co-workers have presented this view in a recent paper, lending it new support by their experimental evidence. The sum and substance of this conception of the mechanism of fever is, that water, which is usually at the disposal of the organism for purposes of heat regulation, becomes not available for this purpose. This may occur by removing a certain amount of water from the organism, or by binding it within the organism in such a way that it cannot exercise its heat-dissipating function by evaporation from the body surfaces

2. Koeppe, H.: Studien zum Mineralstoffwechsel. (1) Wasserretention nach Ernährungsstörungen. *Jahr. f. Kinderheilk.* **73**:9, 1911.

3. Fischer, M.: Edema and Nephritis, 1915, p. 196.

4. Balcar, Sansum and Woodyatt: Fever and the Water Reserve of the Body, *Arch. Int. Med.* **24**:116 (July) 1919.

5. Maver and Schwartz: Studies in Edema in Pneumonia, *Arch. Int. Med.* **17**:459 (April) 1916.

6. Heim and John: Das alimentäre Fieber, *Ztschr. f. Kinderheilk.* **1**:398, 1911; Die Thermoregulation des gesunden und ernährungsgestörten Säuglings, *Jahrb. f. Kinderheilk.* **73**:266, 1911.

7. Peteri, I.: Beiträge zum pathologischen Wesen und zur Therapie des transitorischen Fiebers bei Neugeborenen, *Jahr. f. Kinderheilk.* **80**:612, 1914.

and lungs. In such instances it would be possible to have a water retention and still not enough for proper heat regulation. This may occur in a disease like pneumonia. With restoration of the water-binding power of the tissues to the normal, which may occur more or less abruptly, water would be liberated for heat regulatory purposes and elimination in urine. In this way, the loss of weight coincident or shortly preceding the abrupt fall of temperature, could be explained.

It must be kept in mind that our data are only such as have been obtained in the course of the hospital routine and do not justify us to do further than call attention to this very interesting subject.

PRENATAL SYPHILIS, WITH A PLEA FOR ITS STUDY AND PREVENTION *

JOHN A. KOLMER, M.D., DR.P.H., M.Sc. (Hon.)

Professor of Pathology and Bacteriology in the Graduate School of Medicine
of the University of Pennsylvania; Head of the Department
of Pathology in the Dermatological Research
Laboratories of Philadelphia

PHILADELPHIA

Recent events, and particularly the mobilization and demobilization of troops, has greatly renewed interest in the venereal diseases and aroused considerable concern by reason of their already wide distribution in civilian populations and the danger of further dissemination under existing conditions. Federal, state and municipal health authorities are generally aroused to the dangers of the situation, and are taking steps calculated to limit the spread of venereal diseases, and especially syphilis, and to facilitate their diagnosis and treatment. In this movement all physicians cannot fail to have an interest, and in choosing a subject for this address, I thought the time opportune for bringing before you the necessity of deeper clinical and immunologic study of prenatal syphilis and a consideration of ways and means for reducing the incidence of this disease and thereby reducing infant mortality in general, as well as entering into the general movement against the menace of syphilis.

Excellent reviews on the prevalence of syphilis have been published recently by Vedder¹ and by Stokes;² statistics indicate quite clearly the wide dissemination of this disease. Vedder estimates that from 10 to 28 per cent. of men from the class of unskilled labor and the trades, varying in age from 18 to 40 years, are syphilitic, as well as from 2 to 10 per cent. of men of better education. Among "presumably healthy young women, the percentage of syphilitic infections fluctuates between 2 and 20 per cent., depending on age, marital condition, education and social status. The infection is rare among unmarried girls of good character, but is only too common among married women whose virtue is beyond challenge. As among men, the proportion of infections increases as we descend in the social

* Presidential address delivered before the Philadelphia Pediatric Society, January, 1919.

1. Vedder, E. B.: Syphilis and Public Health, Lea & Febiger, Philadelphia and New York, 1918.

2. Stokes, J. H.: The Third White Plague, W. B. Saunders Co., Philadelphia, 1917.

scale." Evidence indicates that syphilis is far more common among negroes than among whites, and that it is even more frequent among negro women than among negro men; Vedder estimates that the rates for the colored race are at least double those for the white race.

It has been estimated that at least 10 per cent. of all marriages involve a syphilitic individual, and when it is remembered that the disease may be transmitted to children by either parent, and particularly the mother, for an indefinite period, the necessity for obstetricians and pediatricists keeping constantly in mind the subject of prenatal syphilis can scarcely be over-emphasized. Jeans³ recently stated that at least 75 per cent. of all the offspring in a syphilitic family are infected, and 30 per cent. of pregnancies terminate in death at or before term. Thirty per cent. of all infants born alive in a syphilitic family are believed to die in infancy, which is double the normal rate for children in the same class. Only 17 per cent. of all pregnancies in syphilitic families result in living nonsyphilitic children that survive the period of infancy and probably 30 per cent. of clinically syphilitic infants die as a result of syphilis.

Estimates on the prevalence of congenital or prenatal syphilis have been largely based on studies with the Wassermann test; a number of surveys since 1912 have shown positive reactions among from 2 to 6 per cent. of children as met with in dispensaries and hospitals. Studies conducted among backward or mentally deficient and sick children have shown a higher percentage of positive reactions. Very probably about 5 per cent. of children encountered in hospital and dispensary practice will yield positive Wassermann reactions, and it would appear safe to assume an incidence of at least 5 per cent. for syphilis in our infant population, in so far as the disease can be detected by ordinary means.

Without entering into a discussion on ways and means for the prevention of syphilis by the regulation or suppression of vice and education of the individual, my plea is for a closer and deeper clinical and immunologic study of prenatal syphilis on the part of obstetricians and pediatricists. Very probably most can be done toward checking the spread of syphilis, and particularly its transmission to offspring, by subjecting prospective and potential parents to clinical, and especially immunologic, examinations for syphilis, and affording adequate treatment within the means of all, including the poorest of persons, seeking medical aid in our dispensaries.

That prenatal clinics are proving of great value in the conservation not only of infant lives, but those of mothers as well, is now generally

3. Jeans, P. C.: Syphilis and Its Relation to Infant Mortality, *Am. J. Syphilis* 3:114 (Jan.) 1919; also abstr. in *J. A. M. A.* 71:2101 (Dec. 21) 1918.

accepted; I regret that many — probably the majority — of obstetric clinics connected with our teaching institutions neglect the unborn child, being content to register the prospective mother, calculate the probable date of delivery and ascertain the dimensions of the pelvis and position of the fetus. I would urge on all such clinics and on all practitioners practicing obstetrics, the particular study of prospective fathers and mothers for historical, clinical and immunologic evidences of syphilis. This, for obvious reasons, may be difficult and indeed impossible in private practice, but in dispensaries few women will object to an examination of the blood for the Wassermann test if properly handled. An effort should also be made to examine the blood of the prospective father as well, and while this may not be possible on a large scale, it is facilitated by the aid of a social service department.

It has been stated that a man ceases to be infectious within from two to five years after contracting syphilis, depending on the thoroughness of treatment, but that a woman may transmit the disease for an indefinite period; this is probably fallacious teaching in so far as the infectiousness of men is concerned. Fournier,⁴ for example, in a study of 142 men who contracted syphilis prior to marriage and infected their wives, found that twenty-eight, or about 20 per cent., were known to have been syphilitic for from five and one half to eighteen years.

Certainly it would appear advisable, at least, to test the blood of prospective mothers and fathers for serologic evidences of syphilis, and if found positive, provide the means for adequate treatment. In this connection I may state that the Wassermann test is not too delicate, but very probably not delicate enough, and that even with the cooperation of a skilled and trustworthy serologist, a certain percentage of syphilitics will escape detection. A negative reaction, therefore, does not exclude syphilis, because the majority of syphilitic women are in the latent stages of the disease in which the complement fixation test is particularly prone to yield a negative result. The same is true of congenital syphilis, to which further reference will be made. I believe, therefore, in the employment of as delicate a complement fixation technic as is consistent with practical specificity, and that this end is best obtained by the use of cholesterolized extracts for antigens; also that an unmistakably positive reaction may be taken as evidence of the existence of syphilis and an indication for specific treatment.

Furthermore, I believe that it is proper to regard all children as probably syphilitic when born of parents one or both of whom react positively to the Wassermann test, even though both child and parents

4. Fournier, A.: *La Syphilis des honnetes femmes*, Bull. d. l'Acad. d. méd. 66:190, 1906.

are clinically free of the disease; congenital syphilis may manifest itself in so many different ways that the usual clinical picture carried in the minds of the majority of physicians, namely, the child presenting the appearance of "the little old man with a cold in the head" and blebs on the skin, serves for the clinical diagnosis of but a small percentage. As is well known, there may be no discernible lesions and symptoms, and all immunologic tests, such as the Wassermann and the luetin tests, may be negative because so many prenatal infections are with treponemas of attenuated virulence inducing a latent form of the disease, which may not spring into renewed activity for several years after birth. Inasmuch as all evidence indicates that a persistently positive Wassermann reaction means the presence of living treponemas in the body even in the absence of discernible lesions and symptoms, and since the possibility of transmission of these to offspring always exists and particularly from the Wassermann positive mother, I believe that the physician does well to regard with suspicion the offspring of such parents and even to institute specific treatment as a precautionary measure, and especially if such children are manifestly below par in weight and nutrition.

For the study of the incidence of prenatal or congenital syphilis, the Wassermann test alone with the blood of the child is of limited value and cannot be relied on to give complete information. As previously stated, it is prone to yield an erroneous negative result in latent congenital syphilis, although invariably positive in active cases with lesions and symptoms. In my experience, the luetin skin anaphylactic test is of particular value in the immunologic diagnosis of congenital syphilis and an unmistakably positive reaction may be accepted as evidence of syphilis even though the Wassermann test is negative. Such studies should start with the parents and embrace at least the Wassermann test with the blood of the mother and, if possible, of the father, along with judicious inquiries into the previous histories of both as concerns syphilis. Children should be subjected not only to the Wassermann and luetin tests, but to thorough clinical studies, the latter being carried out under best conditions, not by one physician, but, if possible, by several specialists working in cooperation, and particularly an ophthalmologist, a neurologist and psychiatrist and a roentgenologist, inasmuch as syphilis may manifest itself in special organs and thereby escape detection by the general practitioner and pediatricist.

While such studies would prove of great value in emphasizing the importance of syphilis to the individual and the state, and in relation to the important subject of infant mortality, its chief practical object would be lost unless a serious attempt were made to afford adequate treatment for all syphilitics, rich and poor alike. There appears but

one way to reduce the mortality and menace of prenatal syphilis, and that is by the treatment of the prospective and potential syphilitic parent or parents until the danger of transmission is greatly reduced or permanently removed. While health officials and moralists are very properly endeavoring to combat the disease by the eradication and suppression of prostitution and by education of the individual to "mold the desire to live in accordance with the laws of nature," the physician may logically assume that systematic treatment is the only method for reducing the number of venereal infections, and particularly the number of syphilitic infections. Moreover, as stated by Vedder, systematic treatment is the only hopeful and available method for several reasons; it is the one method on which everyone, whatever his or her moral beliefs, can agree, for the morality of the healing of the sick is above suspicion, and no one will challenge the morality of the attempt to treat all venereal diseases. From the sanitary point of view, the treatment of the infected is, perhaps, the most efficacious single method that can be applied, because if all infected individuals are rendered incapable of transmitting their infection the disease will disappear.

I hope that this brief review of so important a subject as congenital syphilis will at least serve to arouse renewed interest on the part of all physicians concerned in the prenatal and the postnatal care of children as obstetricians and pediatricians; it is the disease that should draw both obstetrician and pediatricist into closer professional cooperation, and constitutes an important reason for enlisting the services of the pediatricist in the care of the child before its birth, instead of being turned over to him some weeks or months after this event. The obstetrician alone, and the prenatal clinic, can do most in lowering the high but really unknown percentage of intrauterine deaths of human beings who never had a chance for survival, by adequate treatment of the unfortunate parents; the pediatrician can aid in this work if he is called in time and given an opportunity, and he may do much toward lowering infant mortality by bearing in mind the wide dissemination of syphilis among persons of marriageable age in both sexes, and the imminent danger of transmission to their offspring.

THE ANTINEURITIC AND GROWTH STIMULATING PROPERTIES OF ORANGE JUICE *

ALBERT H. BYFIELD, M.D., AND AMY L. DANIELS, PH.D.

WITH THE COOPERATION OF

ROSEMARY LOUGHLIN, M.S.

IOWA CITY

Orange juice has been so universally regarded as an antiscorbutic, that its other possible properties as affecting the well-being of artificially fed infants have not received much consideration. This, perhaps, is to be expected in view of the fact that the daily giving of orange juice is comparatively recent.¹ Orange juice has been widely used as a mild cathartic for infants and young children, its potency having been assumed. Recently, Gerstenberger² has pointed out that there is no experimental basis for this, and states that, on the contrary, orange juice tends to constipate. The diuretic property of orange juice has been noted by Gerstenberger,³ and again by Hess.⁴ Orange juice was the chief constituent of a fruit mixture used by Gladstone⁵ in treating certain cases of marasmus. This mixture, of which he used a surprisingly large amount—24 ounces a day—consisted of 2 parts of orange and 1 part apple juice with a small amount of water. According to the author's report, this was enjoyed by all babies, who soon became less restless and irritable, but did not gain in weight until a suitable milk modification was given. The good results were attributed to the "tonic cleansing effects on the mucous membranes" and to the "diuretic, diaphoretic and general alterative properties" of the mixture. Kohlbrugge⁶ has reported the benefits following the administration of orange juice in cholera infantum.

The therapeutic effects of the addition of orange juice to the diets of infants suffering from scurvy has been studied by Hess.⁷ Accord-

* From the Department of Pediatrics and the Child Welfare Research Station, State University of Iowa.

1. Hess, J. H.: Principles and Practice of Infant Feeding, Ed. 2, Philadelphia, 1919, p. 156. Hill, L. W., and Gerstley, J. R.: Clinical Lectures on Infant Feeding, Philadelphia, 1917, p. 160. Morse, J. L., and Talbot, F. B.: Diseases of Nutrition and Infant Feeding, New York, 1915, p. 233.

2. Gerstenberger, H. J., and Champion, W. M.: *Am. J. Dis. Child* **18**:88 (Aug.) 1919.

3. Gerstenberger, H. J.: *Am. J. M. Sc.* **155**:253 (Feb.) 1918.

4. Hess, A. F.: *Am. J. Dis. Child*, **14**:337 (Nov.) 1917.

5. Gladstone, H. B.: *Practitioner*, London **97**:472 (Nov.) 1916.

6. Kohlbrugge: *Centralbl. f. Bakteriöl.* **60**:223 (Part 1) 1911.

7. Hess, A. F.: *J. A. M. A.* **75**:1003 (Sept. 18) 1915. Hess, A. F.: *Am. J. Dis. Child*, **12**:152 (Aug.) 1916.

ing to him, some of the symptoms of infantile scurvy appear to bear a close relationship to the deficiency diseases—more particularly beriberi; for besides the usual signs and hemorrhagic symptoms of scurvy, he found such others as tachycardia, dilation of the heart and failure to gain. When orange juice was given, not only did the usual scurvy symptoms disappear, but the children gained in weight and the cardiac signs became normal. The omission of the orange juice was followed by a period of stationary weight until it was again added to the diet. These gains the author attributed to the effect of the antiscorbutic material. In the reports, unfortunately, there are not sufficient data to determine the caloric value of the food given or to indicate its content of growth promoting material. Those children who continued to gain in spite of scorbutic symptoms may have been receiving more food or food supplying more of the antineuritic vitamin.⁸ Our previous work showing the influence on growth of the addition of this vitamin to the diet of babies led us to suspect that Hess' weight gains following the addition of orange juice might be owing to the presence of antineuritic material in the orange juice, rather than to the antiscorbutic material.

Hitherto, oranges, and fruits in general, although valuable antiscorbutics, have not been regarded as sources of the antineuritic vitamin. The literature contains no mention of them in the treatment of beriberi, and with the exception of the banana and the tomato, so far as we have been able to find, there have been no experiments indicating their antineuritic properties.⁹ The present state of our information on this point is suggested by the following quotation from Harden and Zilva:¹⁰ "We have so far not come across a natural product which contained both the antiscorbutic and the antineuritic vitamins in quantities suitable for investigation." In order to obtain a mixture containing both vitamins, these investigators added autolyzed yeast to orange juice to supply the antineuritic material.

Since the antineuritic value of oranges had not been determined, it seemed pertinent to study them from this standpoint, especially in respect to their influence on growth. In our clinic, a series of observations were carried out on babies under the same conditions as those reported in a previous communication.¹¹ With one exception, the diet of the infants was constant throughout the various periods, the intake per kilogram being computed both on the theoretical and actual

8. We shall use the term "antineuritic" vitamin, recognizing the fact that this may include more than one substance as suggested by Mitchell, H. H.: *J. Biol. Chem.* **11**:399 (Dec.) 1919.

9. Daniels, A. L., and Byfield, A. H.: *Am. J. Dis. Child.* **18**:546 (Dec.) 1919.

10. Harden, A., and Zilva, S. S.: *Biochem. J.* **12**:93 (June) 1918.

11. See Note 9.

weights. The milk mixtures were "sterilized" by boiling one minute in an open kettle. In all cases these babies had been receiving from the first month a daily dose of 15 c.c. of orange juice—the customary amount given in this clinic. From preliminary studies of the influence of orange juice on the growth of rats, it was roughly estimated that 45 c.c. of orange juice should stimulate growth. Accordingly, this amount, properly diluted, and sweetened with a few drops of a saccharin solution, was given, one half in the morning and one half in the afternoon, to those infants whose weight had remained stationary for a number of days. For some days previous, and during the observation periods, both the food and the orange juice were prepared by one of us (A. L. D.).

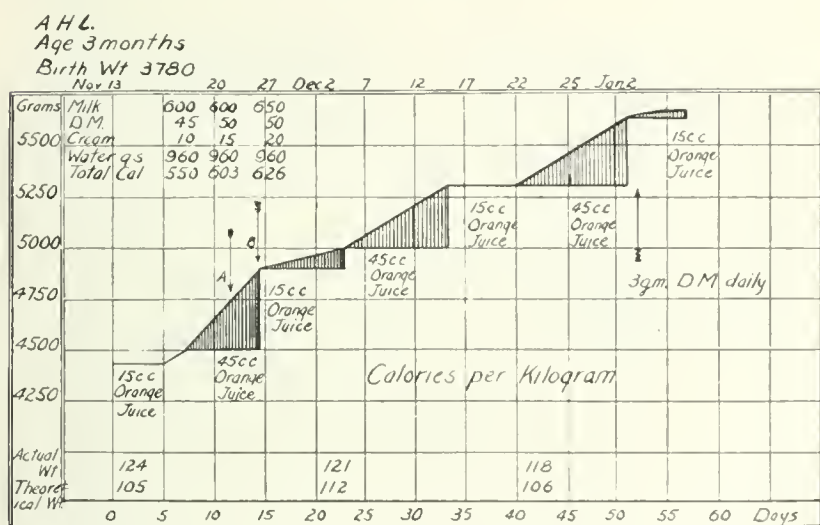


Fig. 1.—A. H. L. Three separate orange juice additions in a period of sixty days gave uniform weight increases. During Period 1, an increase in the food produced no corresponding increase in weight. When the usual quantity of orange juice (15 c.c.) was given at B, a second increase in food was made. The effect of the two food increases was distinctly less than that produced by the larger quantity of orange juice.

It will be noted that in every case when the amount of orange juice was increased from 15 c.c. to 45 c.c. per day, there was a marked stimulation of growth. When the amount of orange juice was reduced to the 15 c.c., the weights again became stationary. The longest observation was in the case of A. H. L. (Fig. 1), three separate orange juice periods being included. During period one it was necessary to increase the amount of food, owing to the fact that the baby was extremely hungry and restless. A food increase of fifty-three calories had no apparent influence on the rate of gain. The day after the orange juice

was removed, the food was again increased by twenty-three calories. This produced only a slight gain (100 gm. in ten days), and was in no way comparable to that produced by the orange juice (250 gm. in five days). The subsequent addition of orange juice during a period of nine days resulted in an increase in weight of 300 gm. A second decrease in the amount of orange juice was again followed by a stationary weight period. A third addition of the larger amount of orange juice stimulated growth as before. The weight curves of the other babies show similar results, and are comparable to those of our earlier work in which it was shown that under similar conditions growth was stimulated by the addition to the milk formula of the antineuritic vitamin obtained from the wheat embryo extract.

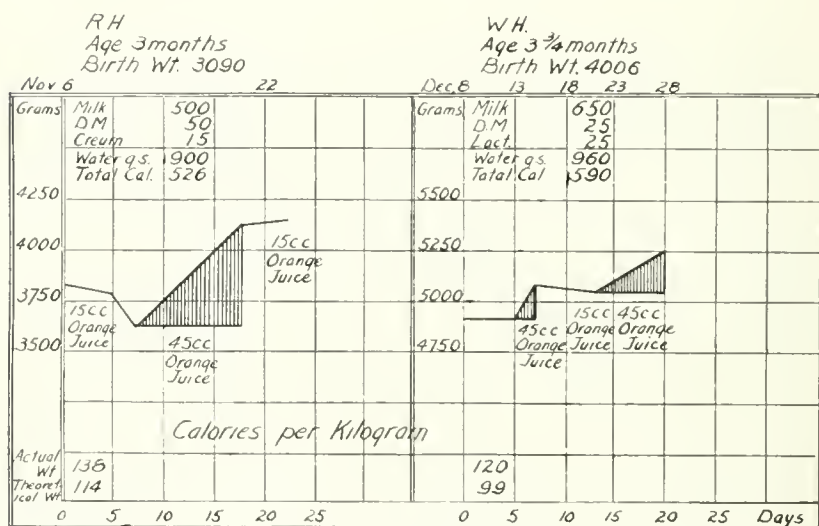


Fig. 2.—R. H. and W. H. The addition of 45 c.c. of orange juice per day produces an average daily weight gain of 40 gm. in the case of R. H.; with W. H. the immediate effect of the addition of orange juice during ten days is shown. A reduction to 15 c.c. produced a stationary weight.

Seidell,¹² and later, Harden and Silva¹³ have shown that the antineuritic vitamin may be removed quantitatively from a substance containing the two vitamins by adsorption, either with Lloyd's reagent or fuller's earth, the antiscorbutic material remaining unaffected. Accordingly, in our work the expressed juice (80 c.c.) of the orange was shaken with 15 gm. of kaolin for twenty minutes and filtered. When 45 c.c. of this filtrate per day were given to the babies there was no increase in weight (Figs. 3 and 4). In the following period, however,

12. Seidell, A.: U. S. Public Health Rep. **31**:366, 1916.

13. See Note 10.

when an equal quantity of *untreated* orange juice was given, there was an immediate gain in weight. From these results it appears that the growth stimulating factor had been removed by the kaolin.

That orange juice contains a growth stimulating material is further evidenced by the fact that rats fed a purified ration, with orange juice as the sole source of the antineuritic vitamin, grew normally, although a larger amount (75 c.c. per 100 gm. of ration) was necessary to produce the same rate of gain as when our wheat embryo extract was used (25 c.c. per hundred grams of ration) (Fig. 5, Group 1). This was not due to the antiscorbutic vitamin because other rats receiving orange juice which had been boiled for five minutes with an excess of a 2 per cent. solution of sodium hydroxid (to destroy the antiscorbutic

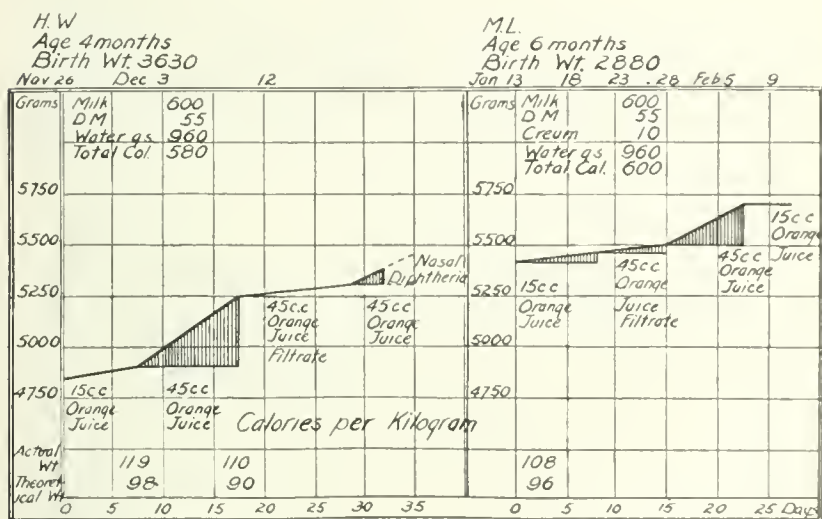


Fig. 3.—Both curves show the comparative influence of the lesser amount of orange juice (15 c.c.), the filtrate of the kaolin treated orange juice (45 c.c.) and of the large amount of untreated orange juice (45 c.c.).

vitamin) grew quite as well as those receiving the untreated orange juice (Fig. 5, Group 2). Furthermore, the addition to a purified ration of the kaolin residue from the orange juice produced a prompt resumption of growth in other animals in which the orange juice filtrate had failed to secure growth (Fig. 5, Group 3, Period 2).

That orange juice contains a considerable quantity of the antineuritic vitamin was also shown by its effect on polyneuritic pigeons. These birds, previously fed polished rice for from twenty-one to thirty-seven days, developed typical polyneuritis, manifested by the classical symptoms—muscular weakness, retraction of the neck, and paralysis of the muscles of deglutition. One of these pigeons, suffer-

ing from almost complete paralysis of respiration, was quite restored by the next morning, after the subcutaneous and oral administration of orange juice on the previous evening. The orange juice, which was injected subcutaneously, was made neutral with sodium hydroxid and sterilized.

The difference in the curative effect of the treated and untreated orange juice was strikingly brought out in two polyneuritic pigeons. One bird, receiving daily 10 c.c. of the untreated juice, recovered in twenty-four hours and showed no polyneuritic symptoms thereafter; the other pigeon, which was given each day 10 c.c. of the filtrate from the kaolin treated orange juice died after four days. A fourth polyneuritic pigeon became so weak that when placed on its side it could

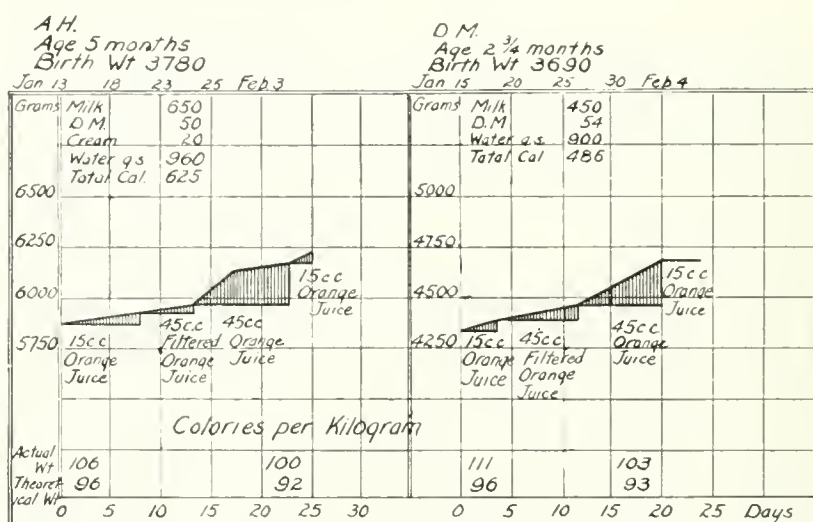


Fig. 4.—The curves also illustrate the difference between the effect of the removal of the antineuritic vitamin from orange juice.

not resume the upright position. It was given 10 c.c. of untreated orange juice by mouth. The next morning the bird was up and about, and apparently quite normal. At the necropsy, the polyneuritic pigeons were found to have full crops and dilated hearts. Some pericardial fluid was present.

To determine the effect of the filtrate from the kaolin treated orange juice, a series of observations were made on both rats and guinea-pigs. Rats (Fig. 5, Group 3, Period 2), fed a purified ration to which this filtrate previously neutralized was added, made no growth, although the amount used was equal to that of the groups fed the untreated and alkalinized orange juice. Guinea-pigs in which scurvy had been produced by a prolonged diet (sixty days) of oats and 40 c.c. of super-

heated milk (100 C. for one hour) per day were cured by the addition of 5 c.c. per day of the filtrate of the kaolin treated orange juice. These facts lead us to conclude that orange juice shaken with kaolin and filtered loses its growth stimulating property, while its antiscorbutic potency is not impaired. Our results, here, are in keeping both with our observations on babies and with the work of Harden and Zilva.

DISCUSSION

The results obtained by the addition of orange juice to or omission from the diet of babies were uniform and constant. Under the conditions maintained, growth, as evidenced by the weight curves, was in all cases stimulated when orange juice was given. On the other hand, orange juice from which the antineuritic vitamin had been removed was without influence. The fact that the changes produced were usually apparent within a day made the results more significant. That

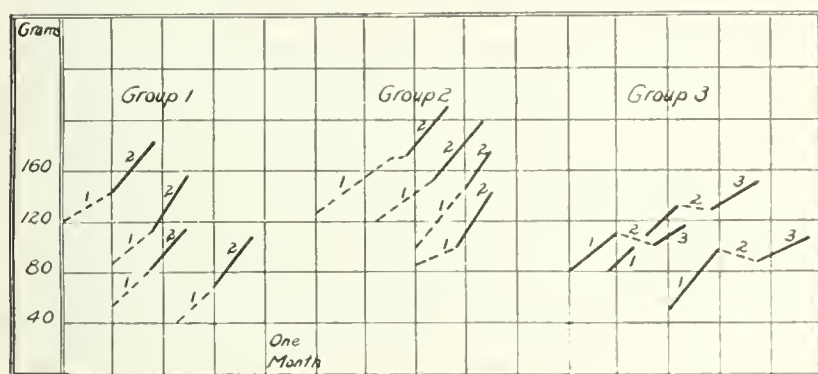


Fig. 5.—This shows the effect on the growth of rats of the addition of the treated and untreated orange juice to a purified ration otherwise complete but lacking the antineuritic vitamin. The ration consisted of 18 per cent. casein, 5 per cent. butter, 23 per cent. lard, cornstarch 46.79 per cent., and 7.03 per cent. of a suitable salt mixture. During Period 1, Group 1, the ration contained 55 c.c. of orange juice per hundred grams of ration; during Period 2, 75 c.c. of orange juice were used. Group 2 was given the alkalized orange juice, 55 c.c. being added to the purified ration during Period 1, and 75 c.c. during Period 2. During Period 1, Group 3 was given the purified ration in which our wheat embryo extract (25 c.c. per hundred grams) was the sole source of the antineuritic vitamin. In Period 2, 75 c.c. of the filtrate from the kaolin treated orange juice was added to the purified ration. During Period 3, the source of the antineuritic vitamin was the kaolin residue of the shaken orange juice.

other constituents of the orange juice, for example, the carbohydrates, apparently played no part in our results is shown in the case of A. H. L. Dietary increases, both during and after an orange juice period, were without marked effect. Furthermore, the addition of 3 gm. of sugar

— dextri-maltose — an amount equivalent to the sugar content of the orange juice of the previous period was also without appreciable effect (Fig. 1). In certain instances the gains were less marked than in others, the greatest gains being made in those babies receiving the most food based on their theoretical weight. If the caloric intake per kilogram—that is, kilogram of estimated weight—fell to ninety or thereabout, there was less stimulation. This is shown in Figure 4.

Up to the present time studies dealing with the influence of the antineuritic vitamin on growth have not shown whether the weight increases were due to the stimulation of appetite, and thus an increased ingestion of food, or to the direct influence of the antineuritic vitamin on metabolism.¹⁴ While not attempting to solve this problem, we have watched our children with this point in mind. In no case was a loss of appetite apparent, the same amount of food being taken during the entire experimental period. In animal experiments the conditions are quite different; for in these considerably less than the minimal requirement of the antineuritic vitamin is usually given for a much longer time. Under these conditions the appetite is greatly diminished; when the antineuritic vitamin, therefore, is added, the effect on the appetite is marked. In our babies' diet, however, a considerable amount of this essential growth constituent was always present, and, therefore, the appetite factor did not seem to enter into consideration. Furthermore, we recall the paralyzing influence of the polished rice diet on the gastro-intestinal tract of the polyneuritic pigeons and wonder if it is not this phenomenon which in animal experiments, in part, at least, is responsible for the anorexia. In general, it appears that the appetite factor plays only a minor rôle in the stimulating effect of the water soluble vitamin on growth, provided a nearly adequate amount is being given.

The question as to whether the antiscorbutic vitamin has growth stimulating properties has not been the subject of extensive experimentation. All authors agree that there is a loss of weight in experimental scurvy, especially as the manifestations become more distinct. There is, however, a corresponding loss of appetite which may be responsible for this. To be sure, in the many observations made by Hess, a failure to gain in children was usual; and in the early stages of the disease, at least, there was no actual loss in weight. Harden and Zilva,¹⁵ and Drummond¹⁶ have reported that rats fed a purified ration to which a small amount of orange juice was added as an antiscorbutic made better gains than others similarly fed but without the

14. Osborne, T. B., and Mendel: *J. Biol. Chem.* **37**:187 (Jan.) 1919.

15. Harden, A., and Zilva, S. S.: *Biochem. J.* **12**:408 (Dec.) 1918.

16. Drummond, J. C.: *Biochem. J.* **13**:77 (May) 1919.

orange juice. They concluded from their work that the antiscorbutic vitamin was essential to the well-being of animals, as manifested by the better weight gains of the rats receiving it. This suggests that the antiscorbutic vitamin has growth stimulating properties. Our own observations on babies, however, fail to bear this out.

At the present time there is little information regarding the coexistence and quantitative relationship in foods of the two water soluble vitamins—the antineuritic and the antiscorbutic. Orange juice has been demonstrated to contain both in appreciable amounts. Similarly, Hess¹⁷ had found that both are present in the tomato. Other foods which have been found to contain both in demonstrable quantities are banana,¹⁸ cabbage,¹⁹ potato²⁰ and turnip.²¹ It is very probable that this list will be greatly extended by further work.

The pathologic similarities of beriberi and scurvy have been pointed out by a number of workers.²² Funk,²³ however, believed that foods which were specific for scurvy also protected against beriberi, although the "beriberi vitamin" was a prophylactic against beriberi only. At that time he did not appreciate that both vitamins might be present in one and the same food. That certain foods, for example milk, contain both vitamins, may also explain the fact that some of the symptoms of both diseases are sometimes present in one and the same individual, the disease type depending on the greater deficiency of the particular food accessory. Thus, similar heart signs and symptoms are described in both scurvy and beriberi. It is possible that the heart symptoms present in those babies who were suffering from scurvy were due, in part, to a lack of the antineuritic vitamin.

CONCLUSIONS

1. Orange juice contains a relatively large amount of the antineuritic vitamin.
2. The growth stimulating influence of orange juice appears to be due to the antineuritic vitamin contained therein.

17. Hess, A. F., and Unger, L. J.: *J. Biol. Chem.* **35**:273, 1919; *Proc. Soc. Exper. Biol. & Med.* **36**:1, 1918.

18. Sugiura, K., and Benedict, S. R.: *J. Biol. Chem.* **36**:171, 1918. Lewis, H. B.: *J. Biol. Chem.* **11**:91, 1919.

19. McCollum, E. J., and Kennedy, C.: *J. Biol. Chem.* **24**:492, 1916. Chick, B., and Mendel, L. B.: *J. Biol. Chem.* **35**:425, 1918.

20. McCollum, E. J., and Kennedy, C.: *Loc. cit.*

21. Osborne, T. B., and Mendel, L. B.: *J. Biol. Chem.* **39**:29, 1919.

22. Chicke, H., and Rhodes, M.: *Lancet* **2**:774 (Dec. 7, 1918). Darling, S. T.: *J. A. M. A.* **63**:290 (Oct. 10, 1914).

23. Funk, Casimir: *Ergebn. d. Physiol.* **13**:124, 1913.

3. Orange juice from which the antineuritic vitamin is removed by adsorption does not stimulate growth. This would seem to indicate that the antiscorbutic vitamin lacks growth stimulating properties.

4. The "pathological affinities" of beriberi and of scurvy may possibly be explained by the fact that the antineuritic content of the commonly used antiscorbutics has not been considered.²⁴

24. After this manuscript had been submitted for publication, we found the preliminary note of Mendel and Osborne (*Proc. Soc. Exper. Biol. & Med.* **17**:46 [Nov. 19] 1919) stating that they were studying the antineuritic content of fruits and had also observed that orange juice contained this growth stimulating material.

FLUID INJECTIONS IN DEHYDRATED INFANTS *

STAFFORD McLEAN AND CHARLES A. LANG, M.D.

NEW YORK

During the summer of 1918 we made an effort to secure some exact clinical data on the effects of introduction of fluids in the case of dehydrated infants. This work was started with the idea of using only the peritoneal route as described by Blackfan.¹ Preliminary to the introduction of his method into routine use, we made a number of intraperitoneal injections in a series of six rabbits. Sixty c.c. of 6 per cent. dextrose solution was used in one group of three rabbits and 60 c.c. of 4 per cent. sodium bicarbonate solution was used in another group of three rabbits. Careful records were kept of the animals after treatment, as to temperature, activity, appetite, etc. In three rabbits we used a solution of 6 per cent. dextrose combined with 4 per cent. sodium bicarbonate. The six animals received forty injections in all. There was one death. This animal died after the third injection of 60 c.c. of a 4 per cent. bicarbonate solution. The necropsy findings were as follows: 25 c.c. of a chocolate colored fluid was found in the peritoneal cavity which showed microscopically a few gram-positive organisms. The culture was sterile. There was no peritonitis and no puncture of the intestines was discovered. The rabbits were caged in a very small room, the weather was very hot with high humidity so that factors other than the abdominal condition may have been the cause of death.

It was our feeling after the experiments with the rabbits that similar injections could be given to infants without causing either injury or discomfort. We prepared to give most of our dehydrated infants fluids by the intraperitoneal route, but in many cases this was not done for reasons having no relation to this study.

A special chart was kept in each ward where the fluids were administered (Fig. 1). In conjunction with the ordinary ward records data relating to the immediate effects of fluids injected were also recorded; these included weight taken before injection and twenty-four hours later and records of pulse, temperature and respiration one half hour before and one hour after treatment. The resident physician observed the child before and after treatment and recorded the effects.

* From the Babies' Hospital.

1. Blackfan and Macy: The Intraperitoneal Injection of Saline Solution, *Am. J. Dis. Child.* **15**:19, 1918.

Only infants showing signs of dehydration were given treatment. Seventy-six infants received 269 injections of fluid. Of these, 155 were hypodermoclyses; ninety-two were intraperitoneal injections, and twenty-two were sinus injections. The mortality in these seventy-six cases was 56.5 per cent.

The amount of the clyses varied between 90 and 150 c.c., depending on the size and condition of the child. In a few cases 1/1,000 to 1/500 grain of atropin was used in the clysis solution. On one occasion, 120 c.c. of a 6 per cent. dextrose solution was used. The intraperitoneal injection fluids were of various formulas, and no attempt is made here to demonstrate different results from different solutions. The amounts varied between 150 and 240 c.c.

The following solutions were used: 6 per cent. dextrose in physiologic sodium chlorid solution; 6 per cent. dextrose in distilled water; physiologic sodium chlorid solution; 2 per cent. sodium bicarbonate with 2 per cent. dextrose solution; 1 per cent. sodium bicarbonate with 1 per cent. dextrose solution.

Fig 1.—Type of chart headings used in all cases.

Age	Name	Diagnosis	Admission Weight	Time of Treatment, Weight	Indications for Treatment	Injection		Clysis, Amount	Pulse		Temperature		Respiration		Weight, 24 Hrs. Later	Results Improved Unimproved Worse	Description of Appearance Following Treatment Etc.
						Sinus, Amount	Intra-peritoneal, Amount		½ Hr. Before	1 Hr. Later	½ Hr. Before	1 Hr. Later	½ Hr. Before	1 Hr. Later			

We have not had any bad results from the intraperitoneal injections, although we have noted discomfort in a few cases.

The clinical diagnoses made in these cases were as follows: Acute ileocolitis, ten cases; acute intestinal intoxication, twenty-six cases; marasmus, eight cases; bronchopneumonia, two cases; feeding cases, fourteen cases; gastro-enteritis, six cases; rumination, pyelitis, marasmus and congenital syphilis, marasmus with furunculosis and peritonitis, marasmus with otitis media, enteritis with bronchopneumonia, hydrocephalus, ileocolitis with bronchopneumonia, acute enteritis and gastro-enteritis with acidosis, one case of each.

In an analysis of the seventy-six cases, there were twenty-six cases of acute intestinal intoxication, or 34.2 per cent.; of all other diseases there were fifty cases, or 65.8 per cent. The mortality in the intestinal intoxication cases was 76.9 per cent., as contrasted with 52 per cent. mortality in other diseases.

In the entire group of cases, 56.5 per cent. of the patients died; 5.2 per cent. were discharged improved; 27.6 per cent. were cured:

5.2 per cent. were removed from hospital against advice; 3.9 per cent. died within a period of two or three days following their discharge from hospital; 1.3 per cent. were discharged unimproved.

The Relation Between the Number of Injections Given Each Child and the Mortality Curve.—In going over these records one is impressed with the bad results in those infants who received three or more injections as compared with those who received less than three injections. In spite of the results noted in Figure 2, it has been found that repeated injections do no harm. One of our patients received as many as thirteen.

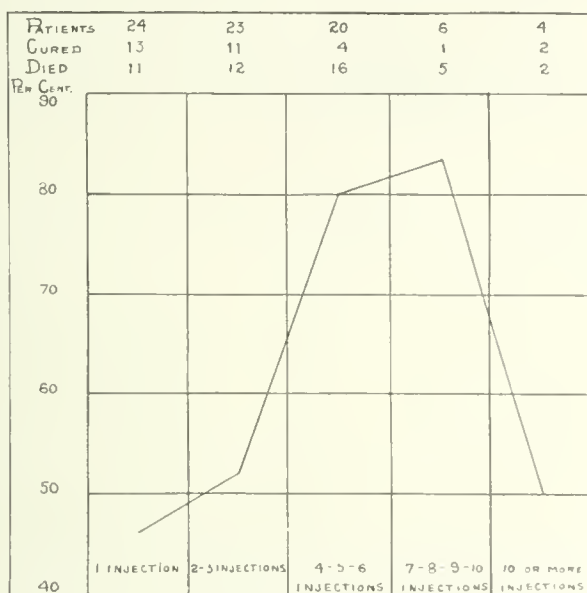


Fig. 2.—Relation between number of injections and mortality.

This series of cases has been grouped into five divisions. In Group 1 are those infants who received one injection. In this group were twenty-four infants, eleven of them died, a mortality of 45.8 per cent. In Group 2 are those infants who received two or three injections, twenty-three cases, with a mortality of 52.1 per cent. Group 3 includes those who had four, five or six injections, twenty in all, with a mortality of 80 per cent. Group 4 includes those infants who received seven, eight, nine or ten injections, six cases, with a mortality of 83.3 per cent. In Group 5 are those who had ten or more injections, four cases, with a mortality of 50 per cent. One notes the lower death rate in the group which had three injections or less as compared with the higher rate in the group which had from four to ten injections.

We are not prepared to say what factors, other than water reten-

tion, influenced the results in Group 1. There are so many conditions which might influence these figures that any conclusions drawn would be purely speculative.

The Relation Between the Weight of the Child and the Mortality Rate.—A glance over these weight records will convince one that the class of cases was not a favorable one. It has been assumed in the past that a very small infant did not react so well to fluid injection as a larger infant. A study has been made here to discover whether this assumption was correct. The infants have been divided into 5 groups.

Group 1, from 2,000 to 3,000 gm. weight.

Group 2, from 3,000 to 4,000 gm. weight.

Group 3, from 4,000 to 5,000 gm. weight.

Group 4, from 5,000 to 6,000 gm. weight.

Group 5, 6,000 and above.

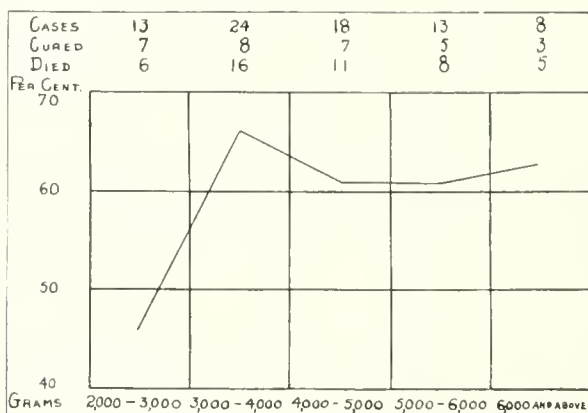


Fig. 3.—Relation of weight to mortality.

It may be noted that the mortality was lowest among the smallest infants, but highest in the next smallest or those weighing from 3,000 to 4,000 gm. If the infants were divided into two groups, and those weighing less than 5,000 gm. placed in one group, and those weighing more than 5,000 gm. were placed in another group, it is found that the mortality in the first group is 57 per cent., and in the second group 61 per cent. From these figures one concludes that there is no definite relation between the weight of the infant and the mortality rate.

It may be noted throughout our series of cases that the weight of the infant bore no exact relation to the amounts of fluid given at each injection. The smallest infants had the lowest mortality rate. It may be possible that they received more nearly their fluid requirements.

The Mortality Curve in Sixty-One Cases with Reference to the Infant's Ability to Retain the Fluid of the First Few Injections.—Our

only means of measuring this was by noting the change in weight following injections. As the infants also received food and fluids by mouth during the same period in which fluid injections were given it will be noted that there were other factors which might have influenced these figures.

The cases have been divided into two groups. In the first group are placed those infants who maintained their body weight or gained weight during the twenty-four hours following the injection of fluids. These include cases in which fluids were given either by clyses, intra-peritoneally or by the intrasinus route. The mortality in the first group was 46.6 per cent.

In the second group are those infants who showed a weight loss twenty-four hours after injection. In this group the mortality was 70 per cent.

TABLE 1.—RELATION OF WEIGHT TWENTY-FOUR HOURS FOLLOWING INJECTION OF FLUID TO MORTALITY

	Cases	Recovered	Died	Mortality	Mortality I and II (combined)
I. Infants with stationary weight 24 hours after injection of fluids.....	7	5	2	28.5%	46%
II. Infants with weight increase 24 hours after injection of fluid.....	23	11	12	52.1%	
III. Infants with weight loss 24 hours after injection of fluid.....	31	9	22	71%	

The Relation Between Age and Mortality.—The seventy-seven cases have been divided into four groups:

Group 1, up to and including 3 months of age.

Group 2, from 3 to 6 months of age.

Group 3, from 6 to 12 months of age.

Group 4, 12 months and older.

There was no marked difference in the death rate of the different groups, but it was slightly lower in the youngest group, namely, 52 per cent.

The Effect on Temperature, Pulse, Respiration and Weight of the Different Kinds of Fluid Injections.—Pulse, respiration and temperature records were taken one half hour before and one hour after injection. The infant was weighed before injection and twenty-four hours afterward. As the vital signs are so easily altered in infants, we have considered a change of ten in pulse rate, five in respiration and of one degree F. in temperature as being definite signs of a reaction. Variations less than these we have not recorded. We have considered 25 gm. as being a definite weight change, any change less than 25 gm. we have not recorded.

Intravenous Injections.—Twenty-one infants received intravenous injections; nineteen of these received 90 c.c. of a 6 per cent. dextrose solution and two received 90 c.c. of a 4 per cent. sodium bicarbonate solution. In ten of these cases, or 47.6 per cent., there was a rise in pulse rate; in seven, or 33.3 per cent., the pulse showed no change, and in four cases, or approximately 19.1 per cent., there was a fall in the pulse rate.

Eight infants, or 38 per cent., had a rise in respiratory rate; in twelve, or 57 per cent., the rate was unchanged, and in one case there was a fall in the respiratory rate.

Eight infants, or 38 per cent., had a rise in temperature; eight, or 38 per cent., had a fall in temperature, and four showed no change.

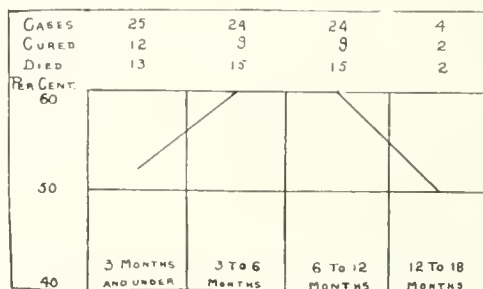


Fig. 4.—Relation of age to mortality.

Of twenty infants, four, or 20 per cent., had a gain in weight; eleven, or 55 per cent., lost in weight, and the remainder showed no change.

Intraperitoneal Injections.—Ninety-nine infants received intraperitoneal injections; forty-seven, or 52.7 per cent., had a rise in pulse rate; nine, or 10.1 per cent., had a fall in pulse rate, and in thirty-four, or 37.7 per cent., no change was noted. In eighty-seven intraperitoneal injections, forty, or 45.9 per cent., had a higher respiratory rate following injection; two, or 2.3 per cent., had a lower rate, and in forty-five, or 51.7 per cent., there was no change. In eighty-six cases studied with reference to effect on the temperature, it was noted that in twenty-seven infants, or 31.6 per cent., there was a rise in temperature following injection; in nineteen, or 21 per cent., there was a fall in temperature, and in forty, or 47.4 per cent., no change was noted. In sixty-five cases studied with reference to the effect on body weight, it was noted that twenty-three infants, or 35 per cent., showed a weight gain twenty-four hours following injection; twenty-six, or 40 per cent., lost weight, and in sixteen, or 25 per cent., there was no change in weight.

Hypodermoclyses.—One hundred and forty-five infants received hypodermoclyses; thirty, or 20.7 per cent., had a more rapid pulse rate; nine, or 6.2 per cent., had a fall in pulse rate, and in 106, or 73.1 per cent., there was no change in the rate.

Of 140 injections, 28 infants, or 20 per cent., had a rise in the respiratory rate; eight, or 5.7 per cent., had a fall in rate, and in 104, or 74.3 per cent., there was no change of rate. Of 140 injections, thirty-eight infants, or 26.9 per cent., had a rise in temperature; nineteen, or 13.9 per cent., had a fall in temperature, and in eighty-three, or 58.9 per cent., the temperature was not affected. Of 131 infants, forty-two, or 32 per cent., showed an increase in weight; in sixty-four, or 48.8 per cent., there was a weight loss, and in twenty-five, or 19 per cent., there was no change in weight. The records in a few cases were incomplete.

A comparison of the effect on pulse, respiration, weight and temperature of the three methods of introducing fluids shows the following:

Pulse: In 47.6 per cent. there was a rise in pulse rate after the sinus injection; in 52.2 per cent. after the peritoneal injection, as compared with a rise of only 20 per cent. after clyses. In 73.1 per cent. of the tabulated cases there was no rise in the pulse rate following the injection of fluid under the skin.

TABLE 2.—EFFECT ON PULSE, RESPIRATION, TEMPERATURE AND WEIGHT

	Sinus Route				Peritoneal Route				Hypodermoclyses			
	Pulse, per Cent.	Respiration, per Cent.	Temperature, per Cent.	Weight, per Cent.	Pulse, per Cent.	Respiration, per Cent.	Temperature, per Cent.	Weight, per Cent.	Pulse, per Cent.	Respiration, per Cent.	Temperature, per Cent.	Weight, per Cent.
Increased...	47	38	38	20	50	45.8	31.0	35	20.5	19.7	28.9	32
Unchanged..	33	57	79	25	37	50.0	47.4	25	72.9	73.3	58.9	19
Drop.....	20	.	38	55	9.2	2.3	21.8	40	6.2	5.6	13.9	48

Respiration: In 38 per cent. respiration was increased following sinus injection as compared with 45.9 per cent. following intraperitoneal injection, and only 20 per cent. after hypodermoclyses. In the intraperitoneal injection a mechanical factor may be operative which has an influence on respiration.

Temperature: In 38 per cent. rise in temperature followed sinus injection as compared with 31 per cent. following intraperitoneal injection, and 26.9 per cent. following hypodermoclyses.

Weight: In 20 per cent. a gain in weight was noted after sinus injection; in 35 per cent. after intraperitoneal injection, and in 32 per cent. after hypodermoclyses.

Figure 5 shows the daily temperature and humidity for July, August and part of September, 1918, indicating the dates of the forty-three deaths which occurred among the patients of this study. We have done this to learn whether there was any relationship between the mortality and weather conditions. The patients are too few in number to serve as a basis of conclusions of this nature. There was a group of six deaths on August 16, 17 and 18. There deaths occurred during a falling temperature and humidity, the humidity on August 16 being 39, the lowest point reached that summer. The temperature on

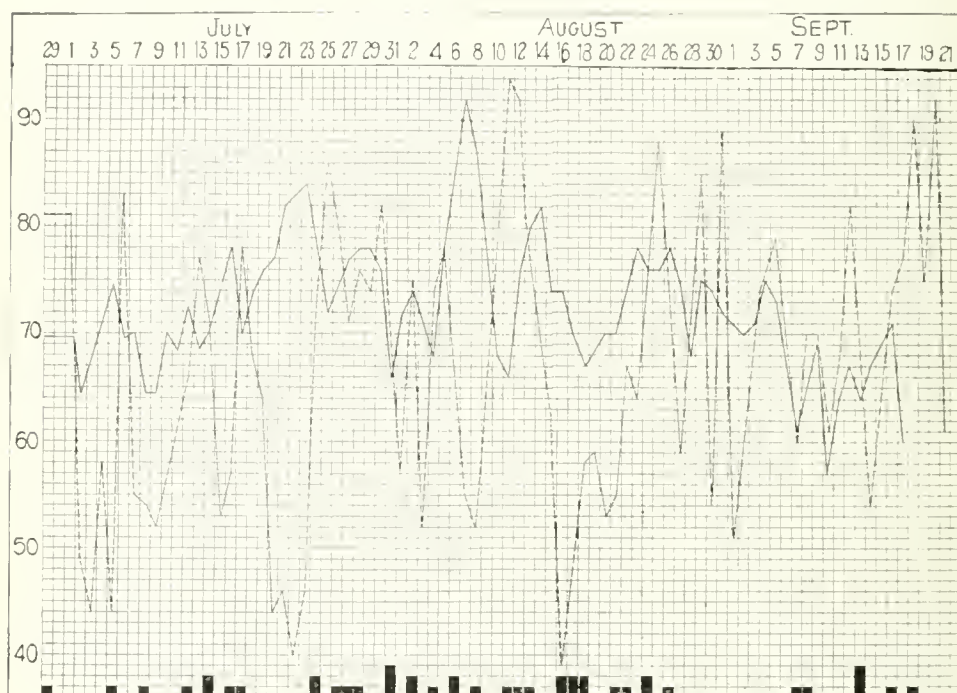


Fig. 5.—Relation of mortality to temperature and humidity. Each black square represents one death. Broken line represents relative humidity; solid line represents temperature.

August 16, 17 and 18 was 70 and 66 F. on the three successive days. This single observation is in keeping with our experience that the sudden fall in temperature and humidity occurring during a period of hot weather has a more harmful effect on the feebler infants than the waves of high temperature and humidity.

Mortality and Duration of Symptoms.—In only thirty-three of sixty-eight cases was treatment begun earlier than ten days after the onset of symptoms. In these thirty-three cases the mortality was 54 per cent. In thirty-five cases the treatment was begun ten or more

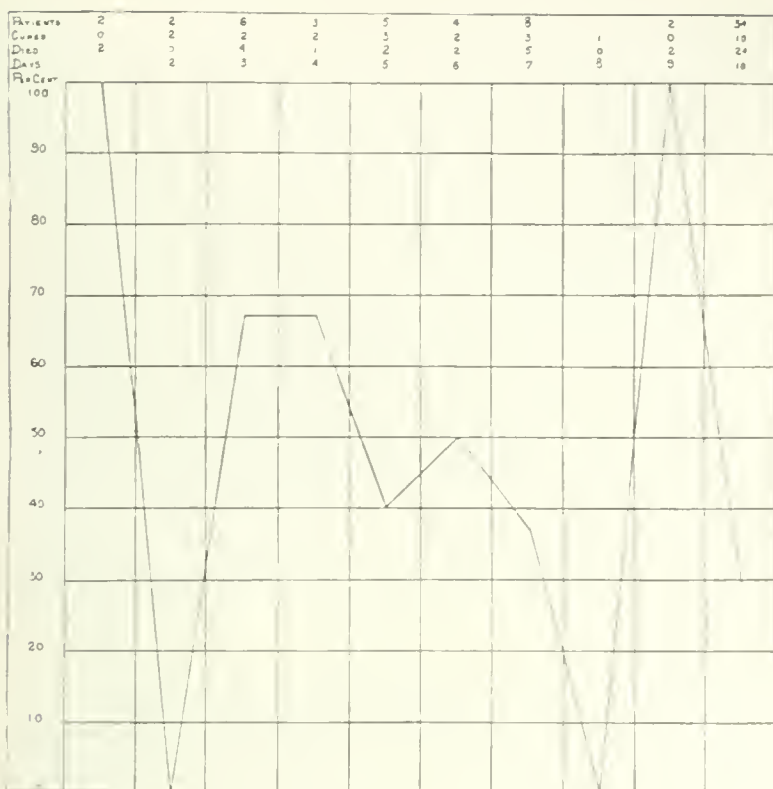


Fig. 6.—Relation of mortality to duration of symptoms.

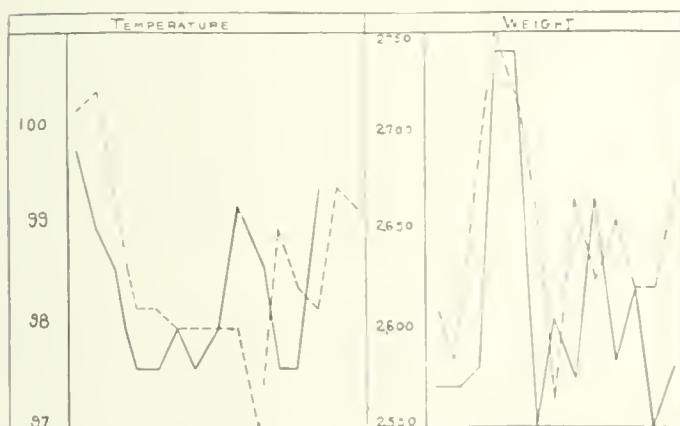


Fig. 7.—Clinical record of a patient who received thirteen saline hypodermoclyses of 90 c.c. each. The solid line represents the temperature one-half hour before injection of fluid and weight at time of injection of fluid. The broken line represents the temperature one-half hour after the injection of fluid and the weight twenty-four hours after injection.

days after onset of symptoms, and in this group the mortality was 68 per cent. It is to be regretted that more cases were not received for admission directly after the onset of symptoms. One of us has recently had a patient admitted to the hospital on the third day after the onset of symptoms. He showed definite evidence of great fluid loss. This child, 20 months old, had his attack begin with diarrhea

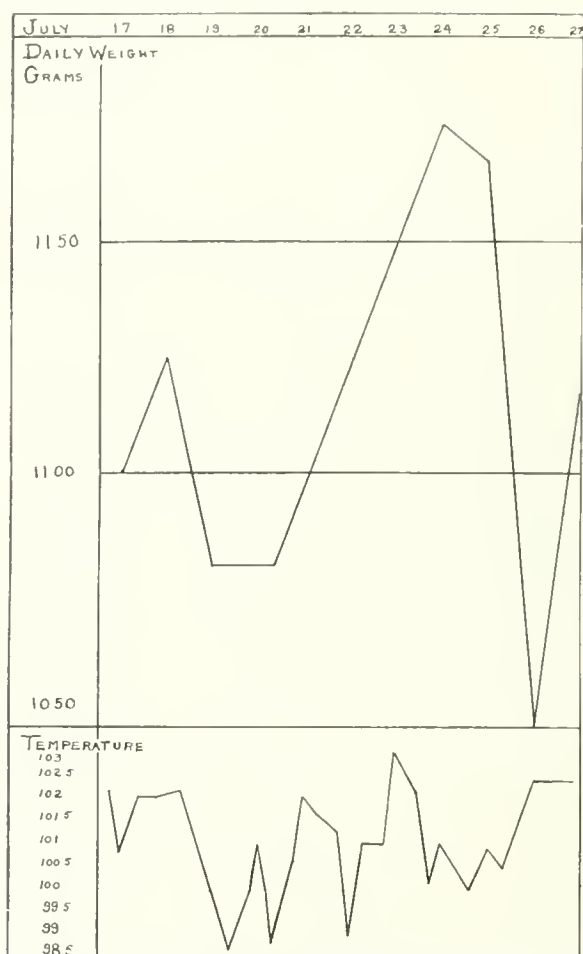


Fig. 8.—Effect produced on weight and temperature by daily intraperitoneal injections of 60 c.c. of a 4 per cent. sodium bicarbonate solution.

and vomiting. His weight prior to the onset was 27 pounds. On the third day, he suddenly became extremely prostrated, and was apparently moribund when admitted to the hospital. The patient was in extreme shock. During a period of eight hours, about 1,600 c.c. of fluid was administered, as follows: 1,200 c.c. physiologic sodium chlorid

solution by clysis; 100 c.c. 5 per cent. sodium solution intravenously; 90 c.c. 5 per cent. dextrose solution intravenously, and 250 c.c. physiologic sodium chlorid solution intraperitoneally. Following directly on this treatment, his condition improved and he was discharged from the hospital apparently well eight days later.

Figure 7 shows graphically the course of one case in which we gave thirteen hypodermoclyses. The patient was cured.

Figure 8 represents the intraperitoneal injections given a rabbit weighing 1,100 gm. It was a male animal apparently normal. The diet consisted of lettuce, oats, carrots and bread, and a constant supply of water was allowed. The rabbit was given intraperitoneally 60 c.c. of a 4 per cent. sodium bicarbonate solution daily for eleven successive days. The temperature was taken three times a day, and daily weighings were made. The animal was as active as the controls during the periods of observation, and the appetite was not affected. His weight on the eleventh day was 24 gm. more than on the day the injections were begun. The weather was intensely hot, and the animal was caged in a small room. Some of the controls, as well as the experimental animal had fever during this same period.

SUMMARY

Injection of fluid into the peritoneal cavity in dehydrated infants is a simple method of procedure and in our hands has had no undesirable effects.

The size of the infant is no bar to his ability to utilize injected fluids.

From the results of injections in very small infants, weighing less than 3,000 gm., we are led to believe that larger infants might utilize larger amounts than have been given to infants in this study.

Age has no bearing on the infant's ability to utilize injected fluids.

The pulse is more frequently affected after sinus and intraperitoneal injections than after hypodermoclyses.

The respiratory rate is more frequently affected in peritoneal injections than in sinus injections and hypodermoclyses.

The temperature is more frequently elevated in sinus injections than in intraperitoneal injections or hypodermoclyses.

Weight gains are more frequently noted following intraperitoneal injections than after sinus injections or clyses.

Certain infants do not show any improvement until they have had repeated injections of fluid.

The shorter the interval between the onset of symptoms and the beginning of treatment the greater is the response.

THE LENGTH OF THE LARGE AND THE SMALL INTESTINE IN YOUNG CHILDREN

LEWIS ROBBIN, M.D.

Assistant Resident Physician, Babies' Hospital

NEW YORK

The not uncommon evidence of an unusually long large intestine disclosed by roentgen-ray examinations of the intestinal tract has evoked very little interest until recent times. Scant reference is made in the literature of the past twenty-five years to the association of such conditions with serious intestinal disturbance. Works on anatomy, as a rule, give only a usual average length for the large and small intestine in adults. The only authority listed in the *Index Medicus* who gives any data on intestinal measurements is Curschman, who, in 1894, published observations on the relationship between the large intestine and body lengths in adults, and described a possible correlation between unusual measurements and the intestinal symptomatology of certain cases.

The observations reported in the present paper are based on measurements made at necropsy of the large intestine, small intestine and body length in 185 children, taken, for the most part, consecutively in the postmortem room of the Babies' Hospital. In the tabulation there have been compared the length of the large and the small intestine with the length of the body, and the length of the large intestine with the length of the small intestine. Record was made in each instance of the age, sex, condition of development and the anatomic diagnosis at necropsy. An investigation was also made to ascertain whether there was an association between any clinical symptoms present during life and the measurements found at necropsy.

The most striking, perhaps the only thing shown in Table 1, is the enormous variation in the length of the large and the small intestine in each of the age periods.

The age periods are too few and the number of cases too small, especially after two years, to determine whether the body grows in length faster than does the intestine. The indications from the average measurements, however, are that it does grow faster than either the large or small intestine at this early period of life.

Tables 3 and 5 give the distribution of cases showing the relation of the body length to the length of the large and small intestine, irrespective of age.

TABLE 1.—AVERAGE LENGTH OF LARGE AND SMALL INTESTINE AT DIFFERENT AGES

Age	Number of Cases	Average Length Large Intestine, Cm.	Range, Cm.	Average Length Small Intestine, Cm.	Range Cm.
0- 1 mo.	25	50.7	30- 80	303.7	140-530
1- 6 mos.	84	59.3	35- 83	384.4	172-520
6-12 mos.	38	70.2	30-110	432.8	230-630
12-24 mos.	26	75.0	55-105	453.5	320-645
24-36 mos.	3	85.7	63-105	403.3	340-440
Over 36 mos.	5	106.0	90-120	468.0	390-560

TABLE 2.—THE AVERAGE BODY LENGTH AT DIFFERENT AGES AND RATIO OF BODY LENGTH TO THAT OF THE LARGE AND SMALL INTESTINE

Age	Average Body Length, Cm.	Ratio Average Body Length to Large Intestine	Ratio Average Body Length to Small Intestine
0- 1 mo.	46.2	1 to 1.09	1 to 6.6
1- 6 mos.	56.5	1 to 1.05	1 to 6.8
6-12 mos.	72.5	1 to 0.98	1 to 6.0
12-24 mos.	75.5	1 to 0.99	1 to 6.0
24-36 mos.	81.0	1 to 1.05	1 to 5.9
Over 36 mos.	101.0	1 to 1.05	1 to 4.6

TABLE 3.—LENGTH OF LARGE INTESTINE COMPARED WITH BODY LENGTH

Length	No. of Cases
From 50 to 60 per cent. of body length.....	1
60 to 70 per cent. of body length.....	2
70 to 80 per cent. of body length.....	7
80 to 90 per cent. of body length.....	27
90 to 100 per cent. of body length.....	37
100 to 110 per cent. of body length.....	49
110 to 120 per cent. of body length.....	35
120 to 130 per cent. of body length.....	20
130 to 140 per cent. of body length.....	4
140 to 166 per cent. of body length.....	2

TABLE 4.—FINDINGS SHOWN IN TABLE 3 SUMMARIZED

Length of Large Intestine	No. of Cases
From 50 to 80 per cent. of body length.....	10
80 to 130 per cent. of body length.....	160
130 to 166 per cent. of body length.....	6

It will be observed that the length of the large intestine was between 80 and 130 per cent. of the length of the body in 91.3 per cent. of the cases; between 50 and 80 per cent. in 5.4 per cent. of the cases, and between 130 and 166 per cent. in 3.24 per cent. of the cases. The normal range of variation may be assumed to be between 80 and 130 per cent. of body length. The other groups would, then, contain what might perhaps be considered unusual or abnormal variations, comprising 8.6 per cent. of the total cases.

No clinical association could be established between the causative factors of illness or death and the measurements in the ten cases in which the large intestine was short. All children died of intercurrent acute infections; seven were males; three were females; the ages ranged between 5 days and 6½ months.

TABLE 5.—LENGTH OF SMALL INTESTINE COMPARED WITH BODY LENGTH

Length	No. of Cases
From 200 to 300 per cent. of body length.....	1
300 to 400 per cent. of body length.....	10
400 to 500 per cent. of body length.....	20
500 to 600 per cent. of body length.....	41
600 to 700 per cent. of body length.....	44
700 to 800 per cent. of body length.....	35
800 to 900 per cent. of body length.....	28
900 to 1000 per cent. of body length.....	3
1000 to 1142 per cent. of body length.....	3

TABLE 6.—FINDINGS SHOWN IN TABLE 5 SUMMARIZED

Length of Small Intestine	No. of Cases
From 200 to 500 per cent. of body length.....	31
500 to 900 per cent. of body length.....	148
900 to 1142 per cent. of body length.....	6

In the group of six cases of the abnormally long large intestine, five were males and one was a female; the ages ranged from 2½ weeks to 10 months. There was a history of chronic constipation in one case, although the infant was always carefully breast fed. Abdominal distention was noted in the physical examinations of three of the patients. A history of chronic intestinal disturbance was given in three cases diagnosed during life as marasmus.

In the measurements of the small intestine, it will be seen that the group in which the measurement was short contains 16.8 per cent. of cases measured; the median group contains 79.95 per cent., and the group of greatest length, 3.25 per cent. of the cases. We may, then, be justified in assuming that any measurement of the small intestine between 500 and 900 per cent. of body length may be considered within

normal range. The other groups might, therefore, be regarded as containing the unusually short and unusually long small intestines.

No association could be discovered between the intestinal measurement and the clinical conditions in either the very short or the very long group. Of the eleven children with short measurements, five were males and six were females. Nine children were well formed and well nourished, and two were poorly nourished. In no case were intestinal lesions associated with nutritional disturbance of long standing.

In the group of six children with unusually long small intestines, four were males and two were females. None gave a history of chronic constipation or chronic distention. Two were premature infants.

An unusual length of one division of the intestinal tract was not necessarily accompanied by an unusual length in the other. In the six cases showing an unusually long large intestine in proportion to body length, the length of the small intestine was within normal range in every case; also in the ten cases showing an unusually short large intestine the measurement of the small intestine was within what we have considered the normal range.

Again, in the six cases in which the small intestine was unusually long the measurement of the large intestine was normal and where the small intestine was unusually short the large intestine relationship was normal.

It is quite evident from these observations that the length of the small and large intestine is subject to very wide variations. The large intestine may be only half the body length or more than one and one half its length. The small intestine may be only three times the length of the body, or it may be eleven times as long. It may be assumed that this difference in the length of the small intestine would not be accompanied by any clinical manifestations. But it is not improbable that an abnormally long large intestine might in later childhood or even in adult life be a condition of considerable importance, especially since the greater part of this increased length is in the sigmoid portion.

SUMMARY

1. The length of the large intestine was found to be between 80 and 130 per cent. of the length of the body in 91.3 per cent. of 185 bodies of infants examined.

2. The length of the small intestine was found to be between 500 and 900 per cent. of the length of the body in 79.9 per cent. of all cases.

3. An unusually long large intestine was not accompanied by an unusually long small intestine; an unusually short large intestine was not accompanied by an unusually short small intestine.

4. No association of an unusually short or long small intestine with the clinical condition could be established.

5. No correlation could be established between an unusually short or long large intestine and the clinical condition. That the anomaly of an unusually long large intestine might be a potential factor in the causation of chronic intestinal indigestion or chronic constipation of later life is worthy of consideration.

6. The indications are that during early life the body grows somewhat more rapidly in length than does either the small or large intestine.

The writer wishes to acknowledge the assistance of Dr. L. Emmett Holt in the preparation of this paper.

TREATMENT OF BIRTH FRACTURES AT FORDHAM HOSPITAL *

SAMUEL W. BOORSTEIN, M.D.

NEW YORK

That fractures do occur during delivery is an established fact. Fortunately, they are not frequent, but these cases cause great anxiety to the physician as well as to the parents.

These fractures are true fractures and not green stick fractures as was believed to be the case, hence deformity must be watched for and guarded against. Truesdell¹ has proven this by his studies.

The first problem is how to treat these children. The methods used in the treatment of fractures occurring in adults are not adaptable for infants. Many surgeons have used different devices for the treatment of birth fractures.

For cases of fracture of the femur Scudder² advises to place the leg in a flexed position on the body similar to the fetal position, the front of the thigh resting on the front of the abdomen, the foot reaching to the shoulder. The trunk is protected by powder and a folded soft towel so that there will be no chafing between the thigh or leg and the body. The position of the lower extremity is maintained by a swathe carefully adjusted or by turns of a bandage. This position is borne well by the child and is maintained for about three weeks. Each day the swathe is removed, the position being maintained while the parts are powdered, the towel readjusted and the leg massaged. Stimson recommended vertical extension of both legs.

Eisendrath³ says: "In children a fracture of the shaft is most easily treated by the use of Schede's vertical suspension."

The Buck and Hodgen splints are not well adapted for use in children.

Speed⁴ advises suspension of both legs at a right angle to the body. The legs are held by Buck's extension attached to a rope and pulley inserted in a longitudinal bar erected over the crib. Enough weight is applied to lift the buttock slightly from the bed surface.

Silver⁵ has combined the use of the Bradford frame and extension in a very useful manner. At a point opposite the hip joint, when the

* From the First Surgical Division, Dr. Alexander Nicoll, Director.

* Read in part before Bronx County Medical Society, May 21, 1919.

1. Truesdell, E. D.: Birth Fractures and Epiphyseal Dislocations, Hoe, 1917.

2. Scudder, C. L.: Treatment of Fractures, Ed. 8, Philadelphia, W. B. Saunders Co., 1918.

3. Keen's Surgery.

4. Speed, K.: Fractures and Dislocations, Philadelphia, Lea & Febiger, 1919.

5. Silver, D.: Surg., Gynec. & Obst., May, 1914, p. 645.

child lies inside the frame, a T connection is tightly screwed into the pipe. To this connection is attached a piece of pipe long enough to reach about four inches above the suspended foot. An L connection, capped at the end, furnishes the termination for this projection. The canvas covering the frame is made from one piece, a hole being cut



Fig. 1.—Fracture of femur. Splint in place, with marked callus present.



Fig. 2.—Fracture of humerus, before application of splint.

for the passage of the upright described. If the surgeon desires to suspend both legs, the frame can be shortened, as it does not have to care for one leg lying extended, and the terminal piece of the upright is longer. Adhesive plaster is used. The leg can be steadied by carrying the diaper around the upright piece or an adhesive strapping can be applied around the groin and the base of the upright.

Russel and Reynolds,⁶ trying to avoid the use of adhesive plaster on the delicate skin of infants, have used the following method for a case of fracture of the femur:

"A plaster saddle was molded to fit the under surface of the knee which was reflexed to form an angle of about 120 degrees with the thigh, and was carried below the foot about $3\frac{1}{2}$ inches to act as a counterweight; this saddle, suitably padded, was bandaged on beneath the knee and suspended from the crossbar of an apparatus constructed



Fig. 3.—Fracture of femur. Good position of femur and much callus.

of a board 13 by 32 inches with side strips 3 inches wide, and with a 21-inch upright at each end, to which was attached a horizontal cross-piece, the suspension being carried out by means of adhesive straps around the saddle, and a cord and pulleys and a 3-pound weight. The extension of plaster below the foot acted as a counterweight to hold the foot down and prevent the saddle from sliding out of position. As there was a slight tendency for the limb to swing from its proper axis after the patient's toilet, etc., had been attended to, a string was attached to the end of the saddle and the latter held in proper position

6. Russel, T. H., and Reynolds, H. S.: Birth Fractures of Femur, *J. A. M. A.* 68:1902 (June 23) 1917.

with slight traction by means of a light weight attached to one of the pulleys. When the limb was suspended the patient promptly fell asleep, evidencing the comfort of the apparatus."

Truesdell¹ devised a box splint for the treatment of birth fractures of the femur.



Fig. 4.—Proper adjustment of the splint to the fractured humerus.



Fig. 5.—Improper adjustment of splint to the fractured femur. This was corrected afterward.

"The splint is built on a base board sixteen inches long, five and one-half inches wide and one inch thick. The sideboards are five and one-half inches high, and cut away for five inches to a height of three inches at the lower end of the box to allow for the band passing over the infant's abdomen to afford countertraction. The upright part of

the splint is sixteen inches long, by two inches wide and one-half inch thick. The upright has an inclination of from ten to fifteen degrees, to bring the flexion of the injured thigh slightly beyond a right angle with the body. It is also inclined sideways to a corresponding degree, to afford abduction of the leg. The inner side of the upright arises from the center of the base board, while the outer side is shaped below to meet the end of the corresponding side-board, thus to strengthen its position. One large or two smaller pulleys are fixed to the upper end of the upright to carry the traction cord, while a screw hook at the base is used to fasten the large elastic band by which the traction is made."



Fig. 6.—Final result in both the fractured humerus and the femur.

All the methods enumerated necessitate keeping the infant constantly in bed and under constant supervision. Scudder's method is, perhaps, easier to carry out, but it also requires a great deal of intelligence on the part of the mother.

On the first surgical division of Fordham Hospital, the surgical director, Dr. Alexander Nicoll, was kind enough to give me the opportunity of treating all the cases of birth fracture. These cases, together with the cases in my clinic in the out-patient department or in private practice, give me an opportunity to report the results obtained.

A new method, or to be more correct, the method introduced during the war for the treatment of fracture of the femur or hand in the adult, was used in all cases. We found it very satisfactory, and in all

the cases in which it was used the method appeared to be quite superior to the other forms of apparatus. We feel justified to advocate its use, so that more extensive studies could be done in that line.

We made use of the Thomas Jones' splint. The method of application is so well known that it needs only a few lines of directions.⁷

The directions are: A strip of adhesive plaster to which a strong loop has been sewn at one end, is applied to each side of the leg or arm. The adhesive plasters should reach from as near the lesion as possible to the malleoli or to the wrist. The lower end of the strip should extend at least 6 inches below the sole of the foot or 4 inches



Fig. 7.—Fracture of humerus; good position of fragments.

beyond the tips of the fingers, and the sticky surfaces are covered with a piece of bandage so that they will not adhere. These ends are now tied to pieces of stout bandage which, in turn, are passed the one over and the other under the wire rods of the splint and returning to the center of the splint they are wound in the opposite direction once around the indentation or notch at the lower end of the splint and are then tied. A small piece of wood, in length about the width of the lower end of the splint, is now inserted an inch or two between the extension bands about 2 inches from the end of the splint, and the amount of traction is increased to any extent by twisting after the manner of a Spanish windlass or the old fashioned link-saw rope.

7. Any book on military orthopedics, fracture or surgery has the directions.

This is retained by catching the end of the wood under or over one of the rods of the splint as the twist requires.

Instead of adhesive plaster we used moleskin plaster, or Sinclair's glue, which does not irritate the skin. The moleskin plaster is so often used in orthopedic practice in treating tubercular joints in children and as it is left on for months without causing irritation, there is no reason why we should hesitate to apply it for a few weeks, even though the patient is an infant.

The peroneal ring is not as tightly applied as in adults, and it is covered with flannel or chamois. The brace extends about 3 or 4 inches beyond the foot. The flannel covering the ring can easily be slipped out and changed every two or three days and the skin be well powdered. To prevent drop foot, a tongue depressor can be placed on the plantar

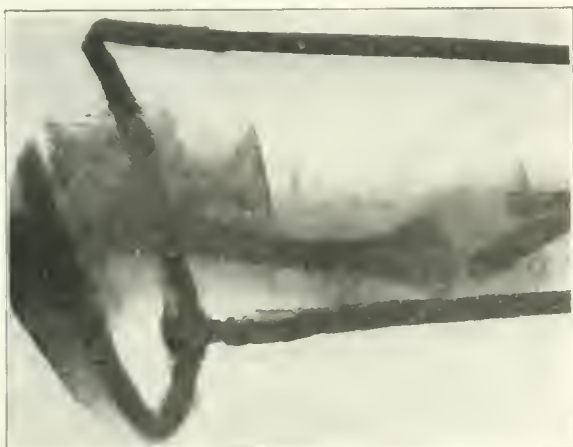


Fig. 8.—Final result; good union and good position.

surface of the foot and held by bandages to the bars of the splint. While wearing the brace, the child can easily be carried around, which means a great deal to the happy mother who is anxious to show the child to the admiring relatives, or to the mother who is burdened with some other important house duties.

A roentgenogram can easily be taken and the results watched. It is also easy to administer massage through the flannel or muslin bandage. The child lifts up the foot together with the brace, and thus the proper voluntary movements are made and union is hastened.

For the upper extremity, the ring is applied to the same shoulder or to the opposite shoulder (the good one). The braces are left on for from three to five weeks. Only two precautions are necessary: (1) The foot or the hand has to be watched for swelling. That can

be prevented if the bands are loosened up once in a while and massaged. (2) The ring must not be too wide, as it will press on the axillary vessels, if the case is one involving the upper extremity, or on the other thigh if the case is one involving the lower extremity, and thus produce a deformity.

The children treated thus far have all done well, both the hospital cases and the ambulatory cases.

I will report a few cases in detail.

REPORT OF CASES

CASE 1.—V. V., one of twins. This was the sixth pregnancy of a poor Italian mother. The delivery was made by a midwife. The infant sustained a fracture of the left femur. It was improperly treated for four weeks. I found no union present, with overlapping of the fragments (Fig. 1). A Thomas Jones splint was applied for two weeks. The length of the leg was increased, but there was still prominence of the upper fragment anteriorly. Under anesthesia the malposition was corrected and the splint reapplied. Massage was resorted to one week later. After three weeks union was good and position good. The child is now $2\frac{1}{2}$ years old and there is no shortening of the limb.

CASE 2.—D. V., fracture of the left femur. The child was brought to the hospital when 4 weeks old. A splint was applied. Massage began one week later. In four weeks she was discharged as cured.

CASE 3.—Becky S., was delivered at the hospital with a fractured right humerus. She was referred to me by Dr. J. Telfair, the attending obstetrician of the hospital. The fracture was at the middle third of the humerus and the upper fragment was displaced upward. A Jones' splint was applied, passing through the good shoulder as a counter extension. The child was discharged after six weeks. No deformity was present (Fig. 2).

CASE 4.—N. M.; second child of a poor Italian family, sustained a fracture of the right femur. It was brought to the clinic when 7 days old. A splint was applied. The mother was permitted to take the child home on the second day and told to report for massage. Discharged after five weeks entirely cured (Fig. 3).

CASE 5.—L. T.; second child; hard labor; placenta praevia; born in the hospital. The case was referred to me by Dr. Telfair, and I saw the child one hour after its birth. There was a fracture of right femur and a fracture of the right humerus. Splints were applied immediately. For the upper extremity the ring passed through the same shoulder. Massage was begun two weeks later. There was only one complication. The ring of the femur splint which we happened to have on hand was a little too wide so that it pressed on the left femur causing a slight curvature. That was corrected with massage (Figs. 4, 5 and 6).

CASE 6.—L. M. C.; born at the hospital with a fractured right humerus. There was no overlapping of fragments. A splint was applied. The patient was discharged cured after four weeks (Figs. 7 and 8).

COMMENT

Of these six cases, three had hospital care, and the splints were watched carefully. The remaining three cases occurred in very poor families where extra care could not be given, still the results were the same. The patients in the hospital gave us the opportunity to observe the methods used carefully, while in the cases of the patients treated at home, the practicability of the method was demonstrated. As a matter of fact, it was proved that it is both safe and convenient to use the splint outside of the hospital. The patients could be dressed easily and carried to and from the dispensary. They could be kept cleaner than under the old methods.

CONCLUSIONS

1. The Thomas Jones splint can be used with safety in cases of birth fractures affecting the femur or the humerus.
2. It allows easier transportation, permits cleansing of the children and saves a great deal of watching.
3. It permits early massage.
4. The deformity is easily controlled.
5. The union probably occurs earlier on account of the ability of the infant to use the limb, to elevate it together with the brace.

I wish to express my thanks to Dr. Nicoll, the director of the first division, under whose auspices the observations and treatments were made, and to Dr. J. Telfair, the attending obstetrician of the hospital for referring the cases so early. I also wish to express my sincerest thanks to Dr. I. J. Landsman, the radiographer of the hospital, for his roentgenograms.

529 Courtland Avenue.

CRANIOTABES AND BEADING OF THE RIBS AS SIGNS OF RACHITIS

HERMAN SCHWARZ, M.D.,

NEW YORK

In applying the new facts in the realm of nutrition and growth to the study of so-called nutritional diseases, it is extremely important to have a sharply defined clinical picture of the cases to be studied before we can make any deductions; therefore, in our chemical studies of tetany, with or without the association of rachitis, in our studies of scurvy, and finally in the study of rachitis itself, we must be positive that we are dealing with the disease under investigation. It is with this idea in mind, that I place on record some observations on craniotabes and beading of the ribs made by me during the past ten years.

It was primarily due to Wieland's¹ work on the clinical and pathologic study of so-called congenital soft heads of infants that my attention was drawn to this phase of rachitis. Since Elsässer² first published his observations on craniotabes in 1843, these soft spots in the infant's skull were thought to be rachitic in origin. However, Friedleben³ soon showed that craniotabes was often present during the first weeks of life. Bohn⁴ followed up some of these cases and thought that the spots present in early infancy disappeared, but those which appeared after the second or third month were really rachitis. Then Kassowitz⁵ published his observations from time to time, adding examinations of pathologic material. He was of the opinion that craniotabes and beading were positive indications of rachitis and could be made to disappear on the administration of phosphorus.

Wieland argued most convincingly that the pathologic examination of Kassowitz's cases frequently showed that the bones were really normal; in some instances, they were syphilitic. Wieland was the first to follow infants who showed craniotabes soon after birth until they reached the second year. He found that these soft places in the skull, often in the dome, sometimes where craniotabes is found in older children, had nothing to do with rachitis.

My patients were examined for the first time a few weeks after birth; then at the third, sixth, ninth and twelfth months. From Table 1 it will be seen that 734 of the 4,944 children showed craniotabes some time during the first year, and that 301 or 6 per cent., had evidences of these soft spots during the first months of life. This number decreases regularly as the infants grow older. It is true, as seen in the

1. Wieland, E.: *Virchows Arch.*, 197, 1909.

2. Elsässer, C. L.: *Der Weiche Hinterkopf*, etc., Stuttgart u. Tübingen, 1843.

3. Friedleben, A.: *Jahrb. f. Kinderh.*, 3, 1860.

4. Bohn: *Jahrb. f. Kinderh.*, 22, 1884.

5. Kassowitz, M.: *Wiener med. Jahrb.* 1884, p. 533; 1879, 1880, 1881; *Ibid.*, *Jahrb. f. Kinderh.*, 69, 1919.

table, that the percentage is larger in the colored race, yet here also the number decreases with age. From this it would appear that at least during the first six months or more, rachitis cannot be diagnosed on the basis of an existing craniotabes. The clinical history of rachitis is certainly against the fact that craniotabes is less prevalent at a time in the infant's life when rachitis is more likely to be present; that is, at the end of the first year. Furthermore, other parts of the body are affected in rachitis, the turgor, musculature,⁶ anemia, constipation, etc. These may become more marked in the infant, yet these soft portions in the skull disappear.

TABLE 1.—CRANIOTABES IN CHILDREN OF VARIOUS NATIONALITIES

Nationality of Parents	Total Number Infants	Infants Showing Craniotabes at Different Months					Total Showing Craniotabes at Any Time	Percentage Showing Craniotabes
		1	3	6	9	12		
American.....	949	39	25	22	6	2	94	12.5
Austro-Hungarian.....	695	51	33	31	8	..	123	16.3
Balkan.....	189	12	10	5	2	..	29	15.3
German.....	142	9	5	9	3	1	27	19.0
Great Britain and Ireland.....	372	14	12	10	6	1	43	11.5
Colored.....	247	45	30	12	10	..	97	39.2
Italian.....	258	13	8	17	7	1	46	17.8
Russian.....	2,292	118	71	73	21	2	275	12.0
Totals.....	4,944	301	194	179	63	7	734	16.5

TABLE 2.—PRESENCE OF BEADING IN CHILDREN OF VARIOUS NATIONALITIES.

Nationality of Parents	Total Number of Infants	Infants Showing Beading at Different Months					Total Number Showing Beading at Any Time	Percentage Showing Beading
		1	3	6	9	12		
American.....	749	103	77	71	57	55	249	33.2
Austro-Hungarian.....	695	93	64	73	60	71	244	35.1
Balkan.....	189	29	16	11	10	14	58	30.6
Colored.....	247	47	49	65	51	64	142	57.4
German.....	142	24	18	20	17	14	57	40.1
Great Britain and Ireland.....	372	46	32	33	39	29	117	31.4
Italian.....	258	32	29	40	36	39	113	43.4
Russian.....	2,292	291	191	203	166	212	749	32.7
Totals.....	4,944	665	469	516	436	498	1,729	35.0

The same applies to beading of the ribs. Table 2 shows that 35 per cent. of all the children present this condition, 13 per cent. during the first month of life, and this proportion changes very little throughout infancy, perhaps, becoming slightly less at an age when rachitis is more common. I am sure that nearly all infants, if examined regularly throughout their first year, will present this condition in a greater or less degree at some time or other in their infancy. It is, perhaps, only when well marked, and in conjunction with epiphyseal enlargement, constipation, anemia, diminished turgor, etc., that it has any significance as a sign of rachitis.

22 East Seventy-Sixth Street.

6. Hagenbach-Burchardt: *Jahrb. f. Kinderh.*, 60, 1904.

ARTIFICIAL INFANT FEEDING

GIVE THE BABY ENOUGH

MAURICE OSTHEIMER, A.B., M.D.

Associate in Diseases of Children, Medical Department,
University of Pennsylvania

PHILADELPHIA

Twenty years of experience in the practice of diseases of children has brought out how prevalent still are the old-fashioned ideas on infant feeding. In fact, after questioning many medical students, I learn that many of these old notions are still being taught; while few of the textbooks change much in regard to feeding, as edition follows edition.

There is the old plan of allowing a new-born infant one ounce every two hours. We know now that the average young infant will always take from three ounces up at each feeding, and can digest it well. Within one week most babies can take four ounces at each feeding; provided, that the interval between feedings is three hours or longer. Anyone who watches a baby at the breast, fed slowly and properly, with a few moments intervals between mouthfuls, which can easily be accomplished by removing the infant from the nipple off and on, knows that he takes three or four ounces, or more, at each feeding. And there is no doubt about his ability to digest it, as is shown by the absence of all symptoms, the well digested stools and the regular gain in weight each week. In spite of this, there still are teachers who give their students the old tables, beginning with one ounce every two hours, for the new-born baby.

Then there is the question "when should the amount of each feeding be increased?" Surely the baby can answer this himself. Just as soon as he can take four ounces well, digest it well and show no symptoms, he should be given another one-half ounce at each feeding; and when he takes that well, still another one-half ounce may be added to his mixture. It is very unfair to order four ounces at each feeding and then forget about it for weeks, as so often happens. It is so easy to omit increasing the baby's mixture unless one's attention is called to it. So many babies, nowadays, are treated thus. I can remember when most bottle fed babies got too much at each feeding. Yet one rarely sees that error now. And this seems especially true among the babies of physicians, usually the most starved of all infants.

Then there is the constant error of keeping the baby on a greatly diluted milk formula, although he may be nine months old or older.

To gain in weight, great quantities of the mixture must be given at each feeding, so we now must have bottles which contain twelve ounces. Surely, we can agree that eight ounces of a stronger milk mixture is far preferable for the baby's digestion.

And again, just as soon as the baby has four or more opposing teeth, he is physiologically ready for some semisolid food. By the age of nine or ten months, then, the modern infant ought to be ready and able to digest undiluted cows' milk, and very soon after that, he should be given cereals, strained at first; potatoes, baked and mashed well; stale bread, toast or zwieback, either hard or soaked in milk or water; stewed fruits, well mashed through the colander, and even a soft-boiled egg.

We have watched infants from 8 to 16 months of age digest these things readily and grow strong, and we marvel at some of the physical specimens presented to us, usually at the dispensary, who have been fed too long on weak milk dilutions and broths.¹

We have watched infant feeding pass through many stages; proteid, sugar and fat have all in turn borne the brunt of the fight. Yet, after all, breast milk remains the one ideal infant food. We know now that the next best substitute for it is cow's milk, certified, which we use, ordinarily, diluted at first with three quarters barley water; then gradually increased up to one half milk. By this time more fat seems needed, and the top twenty-four ounces off of one quart of milk are used; then the top twenty ounces from one quart are employed, still diluted one half with barley water; later whole milk is again used, diluted one quarter with barley water, and so on, increased gradually, until the baby, at nearly 9 months of age, or later, is digesting whole milk, undiluted. It is customary to add about 5 per cent. of sugar to each mixture, that is, 1 ounce to each 20 ounces of mixture.

By this means we simply carry out the idea that young babies, who have been unfortunate enough not to be breast fed, be given sufficient cow's milk mixtures at each feeding, from the very beginning, that each one be allowed an increase in quantity, from time to time, just as soon as they need it. Then, that their mixtures be increased in quality, too, from time to time, until they reach whole milk between 8 and 12 months of age. Then, again, as soon as each one has four or more opposing teeth, he should be allowed to begin on semisolid food.

Such has gradually become our practice in the children's dispensary of the University of Pennsylvania hospital, in marked contrast to the simple, old fashioned diet still advocated by Dr. Morse.²

1. Details of our investigations in this work appeared recently. *Med. Clinics N. America* **2**:841 (Nov.) 1918.

2. *J. A. M. A.* **74**:577 (Feb. 28) 1920.

CLINICAL DEPARTMENT

SUBCUTANEOUS EMPHYSEMA IN AN INFANT THREE DAYS OLD

HAROLD K. FABER, M.D.

Associate Professor of Medicine (Pediatrics) Leland Stanford Jr. University
Medical School

SAN FRANCISCO

Subcutaneous emphysema, occurring spontaneously during the first days of life, appears to be extraordinarily rare. Only two cases have been found recorded in the literature, both reported by Guillot,¹ and even in these there is some doubt as to whether the cause was intrinsic. The Catalogue of the Surgeon-General's Library gives the title of a paper by Lvov² as "On congenital subcutaneous emphysema of the skin," but direct reference to this paper shows that the title should be translated as "The development of cutaneous emphysema during the period of labor," and that the not very unusual emphysema which occurs in mothers during protracted and difficult labor is the subject dealt with. There are a number of reports of subcutaneous emphysema in older children complicating whooping cough, diphtheria and tuberculosis, and a few of emphysema in infants after insufflation for asphyxia or atelectasis. From intrinsic causes, however, emphysema in early infancy is one of the rarities of medicine. Guillot's two cases, summarized briefly, were as follows:

CASE 1.—Girl; first seen when 10 days old; under observation until 41 days old, when she died. The face was congested and sometimes cyanotic. There was an incessant, forcible cough, accompanied by tonic spasm of the extremities and face (trismus), vomiting and convulsions. Auscultation revealed moist râles only.

At necropsy, air blebs were found under the pleura near the hilus and along the bronchi in both lungs. The exact source of the air was not found, but was evidently in the lung proper.

CASE 2.—Girl, first seen when 6 days old; under observation for two days, when she died. There was congestion of the face and rapid, difficult respiration accompanied by incessant, forcible cough. Very fine râles were heard over both lungs. The findings at necropsy were like those in Case 1. The exact site of rupture was not found.

1. Guillot, N.: Observations d'emphysème siéant sous la plèvre, dans le tissu cellulaire des médiastins, étendus jusqu'aux régions du cou, du tronc, de la tête et des membres, que l'on peut attribuer aux efforts de la toux chez les enfants, *Arch. gén. de méd.* 2:151, 1853.

2. Lvov, L. M.: (The development of cutaneous emphysema during the period of labor), *Med. Vestnik* 20:265, 274, 1880.

In neither case is there any note as to the cause. It is possible that insufflation had been practiced by a physician or midwife before the babies were admitted to the hospital.

REPORT OF CASE

The following case was referred by Dr. John A. Sperry, who delivered the mother.

CASE 5.—Girl, born Nov. 2, 1919, first seen by me Nov. 5, 1919.

History.—The mother was a primipara. She and her husband were in perfect health. The day of delivery was two weeks later than the expected date. Presentation was L.O.A. Labor had been in progress fourteen hours. The head was rather hard and had failed to advance after being for an hour at the outlet. Low forceps was applied. Application was perfect and extraction not difficult. There was no unusual degree of traction. Extraction of the shoulders and body was very easy and presented no possible means of trauma. There was no asphyxia, no facial or other paralysis, no evidence of fracture and no sign of trauma, except two very slight forceps abrasions which healed readily without scar. The baby cried normally. Birth weight was 7 pounds 14 ounces. There was the usual postnatal loss of weight which reached its maximum on the third day, after which the baby gained continuously and recovered her normal weight on the eighth day.

During the night of the third day (November 4-5) the baby cried a great deal, not, however, with any unusual force, and was turned over to the prone position. She was left alone in this position for a period of time which we have not been able exactly to determine. On her return, the nurse found on the bedclothes under the face a streak of blood about 6 inches long by 1 inch wide, and noticed that the tip of the baby's nose was severely abraded. The baby had evidently been moving her head to and fro in an effort to get her nose away from the bedclothes and so to obtain free access of air. When seen at this time she was crying vigorously. In the morning, when she was undressed, a swelling of the upper chest and of the neck was discovered.

Physical examination.—Nutrition and color normal. The eyes are somewhat slanting but otherwise normal. Ears normal. There are two nearly healed forceps abrasions, one in front of each ear, unaccompanied by swelling, redness or crepitation. The tip of the nose is abraded and covered with a crust of blood and dried serum. There is no obstruction of the nares, but a faint stridor is heard both in inspiration and expiration. The mouth is normal but the danger from crying or struggling is too great to permit an examination of the pharynx.

There is a symmetrical swelling of the subcutaneous tissues of the neck and chest anteriorly, extending from the lower border of the lower jaw, over the anterior triangles of the neck and the upper central portion of the anterior chest wall, centering over the manubrium sterni and gradually diminishing laterally. The greatest elevation is estimated at about three quarters of an inch. The swelling is unaccompanied by redness or induration; it is quite soft, does not pit on pressure and distinct crepitation is felt on palpation.

No abnormalities in heart or lungs can be detected. Breath sounds are normal in quality and volume and equal in the two sides. No areas of absent breathing can be detected. Facitious sounds resembling crepitant râles when the stethoscope is pressed down are heard over the emphysematous area but there are no râles posteriorly. Abdomen, genitals and extremities are normal. There is no sign of fracture of any of the bones, a particularly careful examination being made of the cranium, bones of the face, the clavicles, sternum and ribs.

Pulse, temperature and respiration are normal. Bleeding time, 90 seconds. Coagulation time, 6 minutes.

Roentgen-ray examination November 6 showed no evidence of fracture of ribs or sternum and, with one exception, none of abnormality within the thoracic cavity. The exception was an area of decreased density, measuring 8 mm. by 15 mm., in the second and third interspaces just to the left of the sternum, which may have represented a collection of air under the pleura or around the main bronchus at the hilus.

Treatment.—Treatment consisted simply in keeping the baby as quiet as possible. She was put in a separate room, in charge of a special nurse, who was instructed to take particular care that the baby should not cry unnecessarily. The room was kept dark. Napkins were changed promptly. If the baby seemed hungry before feeding time she was offered small quantities of a 5 per cent. lactose solution. A supplementary formula of modified milk was offered at feeding time until the mother's milk supply became adequate. It is a tribute to the nursing which this baby received that during the seven days of observation she was hardly once heard to cry. She gained steadily and there was no evidence that any more air was being forced into the tissues. The swelling remained stationary for about three days and at the end of seven days, at which time the baby was taken home, the swelling had diminished by about one half. At the time of discharge, there was no stridor and no evidence of any discomfort or disability. There was no elevation of temperature at any time. No drugs were administered.

Subsequent Course.—I did not see the baby again until Jan. 27, 1920, when she was 86 days old. The mother stated that the swelling had diminished steadily, wholly disappearing by about November 20. It has not reappeared. The baby has made uninterrupted progress on breast feeding. Particular pains have been taken to prevent prolonged or forcible crying, at the expense, it must be admitted, of regularity in the feeding schedule. The baby weighed at the time of the last visit 14 pounds, 6 ounces, an average weekly gain of nearly 9 ounces, and appeared normal in every respect. Nothing abnormal could be detected in chest wall or lungs.

DISCUSSION

It is generally assumed, and doubtless rightly, that the common cause of rupture of pulmonary alveoli is an excessive, sudden rise in intrapulmonary pressure, such as occurs during severe coughing. It is probable that in most cases the lung has already been weakened by disease or by stretching from previous severe or protracted coughing. Normal lung, however, may be ruptured as the result of severe strain. This occurs sometimes in women during childbirth and in babies after insufflation. In the latter case the delicacy of the lung of the newborn child is probably a contributing factor.

It is theoretically possible that a high negative pressure might also cause rupture. Howell³ says of intrapulmonic pressure, "The extreme variations are obtained when the openings to the outside are entirely shut off. When an inspiration or an expiration is made with the glottis firmly closed, the pressure in the lungs, of course, rises and falls with the rarefaction or compression of the contained air. A strong inspiration under such conditions may lower the pressure by 30 to 80 mm. of mercury, while a strong expiration raises the pressure

2. Howell, W. H.: A Textbook of Physiology, Ed. 6, Philadelphia, W. B. Saunders Company, 1917, p. 658.

by an amount equal to 60 to 100 mm. of mercury." Since the maximum negative pressure may nearly equal the maximum positive pressure, there seems to be no reason why alveolar rupture cannot result from the former. It is possible that in the present case the obstruction of the nose from the blood-stained bedclothes was complete or nearly so during inspiratory efforts which would tend to increase the obstruction, but, perhaps, less so during expiratory efforts which would tend to relieve it. If this was actually the case, rupture resulted from excessive negative pressure in the lung.

The careful nursing received by this patient probably saved her life. Guillot's two patients died from an increasing respiratory obstruction which was undoubtedly caused by the progressive escape of air into the mediastinal space, particularly in the narrow thoracic outlet, a condition which was certainly aggravated by coughing and crying. The avoidance of excessive increases in intrapulmonic pressure in the present case was sufficiently complete to allow air absorption to proceed at a greater rate than air escape and so to permit recovery.

PROGRESS IN PEDIATRICS

REVIEW OF THE LITERATURE OF THE PAST FIVE YEARS ON ANAPHYLAXIS AND RELATED PHENOMENA

A. R. CUNNINGHAM, M.D.

Boston Dispensary Research Fellow in Pediatrics, Harvard University

BOSTON

As briefly stated by Weil,¹ a guinea-pig, by virtue of a single injection of alien protein, becomes hypersensitive toward that protein, but by frequent repetition of the same injection, becomes immune. An immunized guinea-pig, on the other hand, possesses a serum which, when injected even in minute amounts into a normal guinea-pig, renders the latter highly hypersensitive to the specific antigen in question.

Up to 1913, according to reviews of preceding literature,² two more or less acceptable explanations of the phenomena of anaphylaxis had been advanced. The first of these hypotheses, the "cellular theory," was advanced by Ehrlich. This supposes that the cells of the body respond to the stimulus of foreign protein by the production of specific immune substances. If large quantities of these substances are produced and are thrown off by the cells into the circulation immunity occurs toward that specific protein. After a single injection of a foreign protein, however, certain animals, notably the guinea-pig, instead of becoming immune, become hypersensitive. It is assumed that in these cases, instead of discharging them into the circulation, the cells have retained their immune bodies, attached to themselves as receptors, and that the antigen, on re-injection, becomes anchored to these cells and so produces toxic or anaphylactic symptoms.

When animals are passively sensitized by the injection of immune serum, it is found that an interval must elapse before these animals become anaphylactic; the injection of antigen during this "incubation period" produces either no symptoms or only slight ones. This phenomenon was interpreted as indicating that the antibodies introduced passively became effective in producing hypersensitization only when they had become anchored by the body cells, and that the "incubation period" represented the time necessary to effect this fixation.

1. Weil: J. Med. Res. **22**:497, 1913.

2. Gurd: J. Med. Res. **26**:205, 1914.

As a corollary to these views, it was assumed that the function of the circulating immune bodies in an immunized animal was simply to bind antigen when introduced, and so protect the body cells with their fixed receptors from attack.

The other hypothesis is known as the "humoral theory." It is based on the fact that guinea-pigs may be poisoned instantaneously, with all the symptoms of anaphylaxis, by means of an injection of a mixture of antigen and of immune serum which has been incubated for a brief period. It assumes that, in a similar way, an antibody is formed in the blood, which, aided by complement, acts as a proteolytic ferment. When only small amounts of antibody are present, as after a single injection, the degradation of the protein introduced in a second injection is incomplete, and toxic proteoses are produced. When large amounts of antibody are present, as after repeated injections, the degradation of the foreign protein, on injection, advances rapidly to a much farther point, resulting in the production of nontoxic end products.

The chief difficulty encountered by this view is the "incubation period," which unquestionably accompanies the typical experiment in passive sensitization. In order to explain this, it is assumed that the "incubation period" represents a temporary period of anti-anaphylaxis due to the simultaneous introduction of traces of antigen which are supposed to persist in all immune serums.

Two difficulties have been encountered by the advocates of the cellular theory; one being that under certain conditions the incubation period can be abolished, and consequently that cellular fixation is an unnecessary assumption. The second was the difficulty in demonstrating that an excess of free immune bodies in the circulation effectively protects the injected animal.

Before reporting his own experimental work, which strongly supports the cellular theory, Weil,¹ in an analysis of preceding literature, throws a great deal of doubt on the evidence that passive sensitization can occur without an intervening period of incubation. He admits that this period may be very short.

In his own experiments, he found it impossible to produce anaphylactic shock in guinea-pigs by injecting antigen and antibody simultaneously. For sensitization to occur, the lapse of an interval of time was necessary between the two injections. The injection of incubated antigen and antibody admittedly produces immediate anaphylactic symptoms, but it has been demonstrated that digestion occurs during incubation, and the degradation products so produced are probably the toxic factors. The hypothetical toxin so produced has been called "anaphylatoxin." Similar symptoms may also be produced by degradation products of proteins obtained by purely chemical methods, and,

therefore, it is evident that the classical symptoms of anaphylaxis are produced by a variety of other forms of intoxication and are not to be considered as by themselves, a true criterion of the state of anaphylaxis. The literature relating to "anaphylatoxin" will be reviewed later in this paper.

To eliminate the humoral factor in anaphylactic shock, several authors report experiments with smooth muscle organs of sensitized and immunized animals after isolating and completely freeing them from blood; Shultz³ showed that sensitization persisted in the bloodless smooth muscle cells of the uterus from sensitized guinea-pigs, when exposed to a solution of the specific protein or antigen. The findings of these experiments were borne out to some extent by similar experiments with immunized animals by Manwaring and others, as quoted by Weil. By the transfer of serum from immunized guinea-pigs to normal animals, and then injecting their serum into other normal pigs, Weil¹ showed by the diminished symptoms in the last guinea-pigs of the series, on injection with the specific antigen, that the quantity of antibodies was apparently diminished by circulation in those first injected, as would be expected if, according to the cellular theory, they had been taken from the circulation by the fixed cells.

By the presence of the incubation stage in animals passively sensitized by the serum of other passively sensitized animals, Weil¹ points out that the explanation of this stage according to the humoral theory, as anti-anaphylaxis due to small traces of antigen present in the immune serum, is unlikely.

Attempts to protect passively sensitized guinea-pigs by the injection of large amounts of free antibodies showed that the protective value of free immune bodies is very low, and that a large excess must be present in the circulation to afford protection against anaphylactic shock. It was shown, however, that this is one of the most important functions of free antibodies. The explanation was advanced that the attached antibodies of the cells had a stronger attraction for the antigen than had the circulating antibodies. Experiments in partly immunized and in anti-anaphylactic animals¹ indicated that these animals contained in their blood enough antibodies to protect against the antigen if brought in contact slowly, as by peritoneal injections, but that if the antigen was injected intravenously, the symptoms of shock occurred. Weil concludes that exactly the same antibodies are present in anaphylaxis as in immunity—in the former they predominate attached to the cells, in the latter they predominate in the serum.

3. Schultz: Bull. Hyg. Lab. U. S. P. H. S., No. 80, 1912; J. Pharm. & Exper. Therap., 1910, p. 549.

Attached to the humoral hypothesis is considerable discussion as to the source of the toxic fraction. Is it derived from the digestion of the protein which is introduced as an antigen, or is its source the protein of the cells of the animal itself? Bronfenbrenner⁴ claims that this poison originates from the serum as a result of its autodigestion and not from the foreign protein. Jobling, Petersen and Eggstein⁵ consider that the acute intoxication is brought about by the cleavage of serum proteins and proteoses through the peptone stage by a nonspecific protease. They explain the mechanism of sensitization and anaphylactic shock in this way: "Serum ferments are practically unaltered by the primary injection of foreign protein. During the course of sensitization, the injection of the antigen is followed by the mobilization of a nonspecific protease which increases in rapidity as the maximum period of intensity is reached. Acute shock is accompanied by the instantaneous mobilization of a large amount of nonspecific protease, decrease in antiferment, increase in the noncoagulable nitrogen of the serum, increase in the amino acids and a primary decrease in serum proteoses. Later, there is a progressive increase in the noncoagulable nitrogen, in proteoses, and in serum lipase. The specific elements lie in the rapid mobilization of a nonspecific protease and the colloidal serum changes which bring about the change in the antiferment tier."

Manwaring, Kusama and Crowe⁶ and Manwaring and Crowe⁷ found that the perfusion of isolated organs and tissues with dilute foreign protein solution furnishes no evidence of measurable destruction of foreign protein by blood serum, nor of appreciable destruction or binding of foreign proteins by the fixed tissues during acute anaphylactic shock. Their findings were borne out by the results of similar experiments by other investigators⁸ and afford no support for either the sessile receptor theory or the theory of humoral protein destruction.

Whipple and Cooke,⁹ however, found that proteose injections in fasting dogs were followed by a rise in nitrogen elimination to more than 100 per cent. above normal. This declined slowly, over a period of from three to five days. They consider their results as evidence of cell injury and considerable protein destruction. Later experiments by the same authors¹⁰ showed a large increase (40 per cent.) in the non-protein nitrogen of the blood, chiefly in blood urea nitrogen but also to a small extent in the amino and peptid nitrogens. The changes in the

4. Bronfenbrenner: *J. Exper. M.* **21**:480, 1914.

5. Jobling, Petersen and Eggstein: *J. Exper. M.* **22**:401, 1915.

6. Manwaring, Kusama and Crowe: *J. Immunol.* **2**:511, 1917.

7. Manwaring and Crowe. *Proc. Soc. Exper. Biol. & Med.* **14**:129, 1916.

8. DeKruif and German: *J. Infect. Dis.* **20**:833, 1917. Aner and VanSlyke: *J. Exper. M.* **18**:210, 1913.

9. Whipple and Cooke: *J. Exper. M.* **25**:461, 1917.

10. Whipple and Van Slyke: *J. Exper. M.* **28**:213, 1918.

blood nonprotein nitrogen are identical with those following the ingestion of large amounts of meat. These facts indicate that the proteose intoxication causes an abnormally rapid autodigestion of tissue proteins, but that the nitrogenous end products are practically the same as those resulting from the normal catabolism of food proteins and probably play no part in causing the intoxication. Weil ¹¹ demonstrates by transfusion experiments that these chemical changes are without influence on the development of shock. They are simply the harmless by-products of the anaphylactic reaction of the sensitized liver, and, as a matter of fact, accompany a variety of pharmacologic procedures which injure the liver, such as chloroform or phosphorus poisoning.

The weight of recently obtained evidence is, therefore, against the humoral theory and rather strongly supports the cellular receptor theory.

Manwaring and Kusama,¹² studying anaphylactic and immune reactions by means of isolated guinea-pig lungs, find that an immune guinea-pig shows apparently a fixed cellular hypersensitiveness, inhibited or protected by humoral or serum immunity. There are three essential factors in anaphylactic phenomena; (a) cellular hypersensitiveness, (b) humoral anaphylaxis, or the response (anaphylatoxin formation) of anaphylactic blood, and (c) humoral immunity—the inhibiting action of immune blood. In the fourteen-day anaphylactic guinea-pig, the fatal bronchial spasm is due partly to fixed cellular hypersensitiveness, and partly to humoral anaphylaxis. In the four-week anaphylactic guinea-pig, the fixed cellular hypersensitiveness is usually greater than in the fourteen-day guinea-pig. The humoral reaction is, however, usually absent. The fatal spasm is usually due to the fixed cellular hypersensitiveness solely. The immune guinea-pig usually shows fixed cellular hypersensitiveness greater than in the fourteen-day guinea-pig. A fatal bronchial spasm is prevented by the inhibiting action of the immune blood. These experiments were borne out by experiments by Moore ¹³ and by Manwaring and Crowe ¹⁴ using the smooth muscle of the guinea-pig uterus after removing all blood and serum.

Anaphylatoxin.—Recently there appeared a summary by Novy and DeKruif ¹⁵ of a series of investigations made by them on the nature of anaphylatoxin. They found that a disturbance similar to what is known as anaphylactic shock can readily be produced by the addition of almost any alien substance to a serum, whether in the living animal or in the test tube. The substances which they mention include bacteria, trypanosomes, organ cells and extracts, peptone, agar, starch, inulin, kaolin,

11. Weil: J. Immunol. **2**:399, 1917.

12. Manwaring and Kusama: J. Immunol. **2**:157, 1916.

13. Moore: Proc. Soc. Exper. Biol. & M. **12**:175, 1915.

14. Manwaring and Crowe: Proc. Soc. Exper. Biol. & M. **14**:129, 1917.

15. Novy and DeKruif: J. A. M. A. **67**:1524, 1917.

silicic acid, barium sulphate, diverse salts and even distilled water. The result is a nonspecific anaphylactic shock, to be distinguished from specific anaphylactic shock in which the inducing substance is formed by the interaction of the antigen with its antibody. They also concluded that the poison produced did not come from the substance introduced, but that its matrix was always present in normal serum, and that the substances which convert it into anaphylatoxin act merely as inducers or accelerators of this reaction. Since shock blood is incoagulable, they assume that this inducing substance also reacts with fibrinogen. All bloods are toxic in the precoagulation stage—thus the blood of a normal rabbit when rapidly transfused into the vein of a guinea-pig, is usually harmless in a dose of 3 c.c. If, however, the blood is held in the syringe for three minutes before injecting, it becomes fatally toxic. The effects produced are those of anaphylatoxin. The production of anaphylatoxin varies in different species of animals and in different individuals. The two reactions—blood coagulation and blood toxification, are twin phenomena in which labile substances undergo intramolecular rearrangement. In one case, the insoluble fibrin is produced, and in the other, the soluble anaphylatoxin. There is no good reason to believe that anaphylatoxin is formed by the hydrolysis of a matrix.

Weil¹⁶ takes the position that these reactions are in no way related to true anaphylaxis. "Anaphylaxis, meaning the reaction of a previously treated animal to (fresh) injections of antigen, is always and invariably mediated by the cellular antibody and by that alone."

Other Views of Anaphylaxis.—In one of his earlier papers Novy¹⁷ advanced the suggestion that anaphylactic shock was the result of a disturbance of the colloidal state of the plasma constituents caused by the alien material introduced. In two papers Krichewsky,¹⁸ injecting the sap of cotyledon *Scheideckeri*, concludes that the cause of anaphylactic shock and death is a change in the degree of disperseness of plasma colloids.

Soula,¹⁹ Klinkert,²⁰ and others, consider that anaphylaxis is a result of the action of poisons on the nervous system. Soula finds a distinct modification of the lipid formula of the nerve centers, in the course of sensitization, and considers the humoral reaction as secondary. Klinkert considers that the nervous system in anaphylaxis is exceptionally sensitive.

Relation of Anaphylaxis to Precipitin, Agglutinin and Complement Fixation Reactions.—In studies to determine the relation of precipitin

16. Weil: J. Immunol. **2**:109, 1916; **2**:399, 1917.

17. Novy and DeKruif: J. Infect. Dis. **20**:409, 1916.

18. Krichewsky: J. Infect. Dis. **22**:101, 1917.

19. Soula: Presse méd. **24**:471, 1916.

20. Klinkert: Nederl. Tijdschr. v. Geneesk. **1**:941, 1918; **1**:202, 1917.

to sensitizin (the anaphylactic antibody) Weil²¹ concludes that both are properties of the same substance. This substance loses the precipitating property upon heating but does not so lose the sensitizing property. The antigen and the precipitating antibody do not coexist in the same fluid without undergoing union and precipitation. Other results may be obtained, however, when the antigen used consists of mixed substances. Outside the body, precipitates may contain both antigen and antibody, but their coexistence in a precipitate does not prove their coexistence in the body.

Lake, Wells and Osborne²² produce evidence to show that the precipitin, agglutinin, complement fixation and anaphylactic reaction all represent the interaction of the same specific immune body with its corresponding antigen, the different reactions being merely different methods of demonstrating the presence of this antibody.

In comparing the phenomena of complement fixation and anaphylaxis, Kahn and McNeil²³ find that whereas a fraction of a milligram of antigen may suffice to produce anaphylactic antibodies, the production of complement fixation antibodies requires a much larger amount of protein. Gelatin, which lacks cystin, tyrosin and tryptophan, and which has been shown to lack anaphylactic properties, also fails to produce fixation. This seems probably to be due to its deficiency in aromatic radicals which have been shown by a number of workers²⁴ to appear particularly important in immunity reactions. Mere lack of certain amino acids does not prevent a protein from becoming an antigen. As in other immunity reactions, specificity of the complement fixation reaction depends on the chemical structure of the protein molecule, and if the molecule be split its specific complement binding power is lost.

Specificity.—Wells and Osborne²⁵ found that the pure hordein of barley would produce an anaphylactic reaction in a guinea-pig sensitized to pure gliadin of wheat, which is chemically related but distinct in formula. It also produced a reaction in a guinea-pig sensitized to pure gliadin of rye, which is chemically the same as that of wheat. These reactions were not as strong as those produced by the homologous protein. They conclude that this indicates either the presence in gliadin and hordein, of two or more individual proteins, one of which is common to both, or that both contain a common chemical reactive group. Chemical evidence favors the latter assumption. Probably the entire protein molecule is not involved in the specific character of the anaphylactic reaction, but this is developed by certain groups contained

21. Weil: J. Immunol. **1**:1, 19, 35, 47, 1915.

22. Wells, Osborne and Lake: J. Infect. Dis. **24**:364, 1913.

23. Kahn and McNeil: J. Immunol. **3**:277, 1918.

24. Well's Chemical Pathology, Ed. 2, 1914, p. 179.

25. Wells and Osborne: J. Infect. Dis. **12**:341, 1913.

therein. One protein molecule may contain two or more such groups which determine the specificity. The possibility still remains that so-called "pure proteins" really consist of mixtures, and that an individual protein rather than a group of the protein molecule determines the specificity. The same authors²⁶ show evidence that the solubility of vegetable proteins in the body fluids (peritoneal) is an important factor in determining the severity of the reaction. The more soluble, the more severe is the reaction. Zinsser and Parker²⁷ found that this is also true of bacteria and red blood cells. Whole bacteria or whole red corpuscles do not cause a reaction in the sensitized uterus; the reaction only occurs when they are added in the form of an extract or solution.

Wells and Osborne²⁸ state that protein substances are found in many grains and seeds, which, on account of their solubilities, have been designated as "proteoses." Since artificial proteoses produced by the tryptic digestion of egg-white, and other lower products of hydrolysis, do not sensitize guinea-pigs, it is evident that these natural substances which exhibit strong anaphylactogenic properties in guinea-pigs belong to a group of proteins chemically distinct from any previously recognized, and that their designation as "proteoses" is consequently improper.

Rôle of the Lungs in the Anaphylactic Reaction.—The lungs show three types of anaphylactic reaction: ²⁹ (a) bronchial, or the spasmodic contracture of the bronchial musculature unassociated with recognizable changes in the pulmonary blood vessels; (b) vascular, or the spasmodic contracture of pulmonary blood vessels usually accompanied by edema, and usually followed by a mild bronchial reaction; (c) pseudo-anaphylaxis, or the plugging of pulmonary blood vessels with thrombi. These types are found in animal experimentation. Pelz and Jackson,³⁰ from experiments with highly sensitized and pithed dogs, feel certain that the asphyxia produced by the acute bronchial constriction, may readily be the cause of death. These phenomena occur with the liver and other abdominal viscera wholly removed from the circulation.

Rôle of the Liver. Since it has been suggested that cases of food sensitization receive their antigenic doses of protein through a too permeable intestinal wall which permits the passage of the specific protein in an insufficiently digested state, it will be of interest to consider the action of the organ which receives directly through the portal

26. Wells and Osborne: J. Infect. Dis. **14**:377, 1913.

27. Zinsser and Parker: J. Exper. M. **26**:411, 1917.

28. Wells & Osborne: J. Infect. Dis. **17**:259, 1915.

29. Manwaring and Crowe: Proc. Soc. Exper. Biol. and M. **14**:173, 1916.
Coca: Proc. Soc. Exper. Biol. & M. **16**:47, 1917.

30. Pelz and Jackson: J. Lab. & Exper. M. **3**:387, 1918.

system, a large share of the mesenteric blood, and which has an important part in the metabolism of protein.

Portal blood³¹ goes from the capillaries of the intestines to the liver without aeration or contact with other tissues. In the passage through the intestinal villi, it comes in contact with many cells whose function is to absorb and throw into the blood the various products of tryptic digestion. Probably, also, proteolytic ferments are absorbed and carried to the liver.³² It is also probable that the carbon dioxide tension is greater in the portal blood than in the peripheral blood because of the decreased pressure and slower circulation. This condition would tend to increase the rate of proteolysis. It is not definitely known whether protein molecules are completely broken down to the end-products of tryptic digestion before absorption, or whether large fragments of molecules may not be carried to the liver and there broken into amino-acids before entering the peripheral blood. The liver is probably rich in ferments as shown by the rapid postmortem autolysis. For these reasons protein substances might be expected to produce atypical reactions of anaphylaxis when introduced into the portal rather than the peripheral circulation. It was assumed by Abderhalden as quoted by Falls,³² that the liver is a buffer between the intestinal and the general circulation and protects the latter from the entrance of foreign proteids which, when incompletely digested, would have poisonous potentialities.

Falls finds that guinea-pigs may be sensitized by intraportal injections of human serum with resultant anaphylactic shock after either peripheral or intraportal subsequent injection. Larger doses are necessary when the shock dose is administered intraportally, irrespective of whether the sensitizing dose is given thus or peripherally.

Manwaring and Crowe³³ perfused the isolated organ with solutions of dilute foreign protein and tested the resulting changes in the toxicity of the perfusion fluid by subsequent perfusions of isolated anaphylactic lungs. They found that the liver of a normal guinea-pig produces little or no change in the toxicity of the perfusion mixture for the anaphylactic lungs on subsequent perfusion, were thrown into a typical anaphylactic response. Repeated perfusion of the anaphylactic liver, on the other hand, invariably results in reducing the toxicity of the perfusing fluid when the protein is diluted in normal blood. This reduction, however, is never as complete as when the liver is anaphylactic, and the foreign protein is carried in anaphylactic blood. In these experiments, the perfusion fluid usually completely or almost completely loses its power to produce an anaphylactic response when later tested with

31. Falls: *J. Infect. Dis.* **22**:83, 1917.

32. Falls: *J. A. M. A.* **65**:524, 1915.

33. Manwaring and Crowe: *J. A. M. A.* **69**:772, 1917; *Proc. Soc. Exper. Biol. and M.* **14**:174, 1917; *J. Immunol.* **2**:517, 1917.

anaphylactic lungs. Furthermore, on repeated passages through the anaphylactic liver, the perfusion fluid also acquires a new power, that of causing an unusual relaxation in the pulmonary tissues. There is also a loss of the occasional power of the perfusion fluid to cause vasoconstriction. The detoxicating effect of the anaphylactic liver is therefore accompanied by, and is possibly due to, the explosive formation and liberation of vasodilator and bronchodilator substances. Similar findings were obtained by Simonds.³⁴

As contrasted with guinea-pigs, in which the cellular reaction of anaphylaxis affects chiefly the smooth muscle cells, in dogs it is a cellular reaction the chief site of which is the hepatic parenchyma. Weil³⁵ states that in dogs all features of anaphylactic shock appear to be due to the direct effect of the antigen on the sensitized liver. Simonds³⁶ demonstrates the congestion of the liver in anaphylactic shock in these animals, and the resulting incoagulability of the blood. The congestion of the liver appears adequate to account for the fall in blood pressure. Proteolytic changes appear in the blood similar to those accompanying other forms of hepatic injury such as chloroform or phosphorus poisoning.

Other Pathology.—According to several authors³⁵ eosinophilia is present in anaphylactic shock.³⁶ Boughton³⁷ finds lesions of the smaller arteries of the liver, kidney, spleen and heart, after repeated injections of foreign protein in sensitized guinea-pigs. These are most prominent in the liver and spleen. The same author³⁸ finds that repeated anaphylactic shock in guinea-pigs is able to produce lesions of the kidney that are not produced by acute anaphylaxis alone. These lesions are characterized by necrosis and swelling. The site of the chief disturbance in shock apparently varies in different species, in the guinea-pig affecting the smooth muscle especially of the lung tissue, and in the dog, the hepatic parenchyma, producing marked congestion.

Human Sensitization.—Heredity: Cooke and Van der Veer³⁹ made an extensive investigation of this subject. They found conditions probably anaphylactic in nature in the family history of 48 per cent. of 504 sensitization subjects, while in seventy-six normal persons this history was obtained in only 14 per cent. In patients with a double heredity the period of maximum liability occurs in the first five years when 36 per cent. of forty-four persons developed it. In persons having only a single inheritance of this sort, this period is from ten

34. Simonds: J. Infect. Dis. **19**:753, 1916.

35. Weil: J. Immunol. **2**:525, 1917.

36. Schloss and Worthen: Am. J. Dis. Child. **11**:342, 1916.

37. Boughton: J. Immunol. **2**:501, 1917.

38. Boughton: J. Immunol. **1**:105, 1916.

39. Cooke and Van der Veer: J. Immunol. **1**:201, 1916.

to fifteen years. In patients without heredity, the height of the curve is not reached until the age of 20 or 25. The offspring of a sensitive patient is, however, not born sensitive; the clinical form in children is much more apt to differ from that of the parent (45 per cent.) than to be identical (18 per cent.), and it is to be concluded that sensitized individuals transmit to offspring not their own specific sensitization, but an unusual capacity for developing reactivities to any foreign protein. Sensitization is inherited according to mendelian laws as a dominant trait.

Many of their cases showed multiple sensitization. They did not find that artificial sensitization is easy to accomplish and horse serum was tested in this respect. Evidently the type of clinical sensitization that is naturally acquired and maintained is dependent on some other factor than mere parenteral injection.

Tests of Protein Sensitization.—Various methods are in use for determining the presence of protein sensitization in human beings. In tuberculosis the specific tuberculin is brought into contact with the serum by the cutaneous or the intracutaneous method, or by instillation into the eye. It has been demonstrated by Bass⁴⁰ that the intracutaneous test is more sensitive than the ordinarily used cutaneous method. This intracutaneous method has also been adopted in testing for the presence of diphtheria antibodies. Walker and Adkinson⁴¹ consider the cutaneous method to be preferable in testing for protein sensitization in asthmatics and hay-fever patients. They find that this test is specific, not too sensitive, and separates closely related proteins, and that it serves as a safe index to the dosage to be used in immunization. The intracutaneous test is too sensitive to be specific or a valuable index to treatment. In Study XIII⁴² and Study XV⁴³ the author concludes that in the failure of cutaneous tests, serum agglutination tests were of value in a few instances, especially of *S. pyogenes aureus* sensitization. No serum agglutinates *S. pyogenes albus*. In Study XII,⁴⁴ Walker, from a series of patients with bronchial asthma, concludes that complement fixation and precipitin reactions have no value in diagnosis, prognosis or treatment.

The cutaneous test is performed with pure proteins soluble in dilute alkali solutions. A cut one-eighth of an inch long and not deep enough to draw blood, is made in the skin, through a drop of decinormal sodium hydrate solution. A small amount of blood is not of consequence. A small quantity of dry powdered protein is then mixed with the drop

40. Bass: Am. J. Dis. Child. **15**:313, 1918.

41. Walker and Adkinson: J. M. Res. **37**:287, 1917.

42. Walker: J. M. Res. **37**:51, 1917.

43. Walker: J. M. Res. **37**:951, 1917.

44. Walker: J. M. Res. **36**:243, 1917.

of alkali, and thus, in solution, comes in contact with the serum of the patient. The occurrence of a wheal and reddening constitutes a positive reaction. The intracutaneous test consists in injecting a solution of protein into the skin. Strickler and Goldberg⁴⁵ consider this reaction not positive unless it persists for forty-eight hours, and they believe that this element of time constitutes the most important factor in determining a positive reaction. Next to the element of time, infiltration, or the presence of a papule, is most necessary, and lastly erythema. They conclude that these reactions, when interpreted properly, are a valuable guide in determining dietary factors operating in the production of diseases of the skin. They are specific, but a positive one does not necessarily indicate that the disease is due to the food giving the positive reaction.

Tracey⁴⁶ describes the normal reaction of the skin to stroking.

The methods of preparation of pure proteins suitable for such tests have been described by Wodehouse,⁴⁷ Ferry,⁴⁸ Baker and Floyd,⁴⁹ and Goodale.⁵⁰

Clinical Forms of Anaphylaxis.—Simpson⁵¹ in work on primrose dermatitis, makes a valuable comment bringing out the true relations and nature of anaphylaxis in clinical work. Quoting Richet, he states that it was shown in 1898 that anaphylaxis depends on the previous injection into, or the presence in the body, of some sensitizing substance. Another demonstrated fact is that such an exciting substance must be of a protein nature. In support of this he cites Miller,⁵² Richet,⁵³ Thiels⁵⁴ and others. Therefore, it is to be remembered that drug hypersensitiveness, or poisoning by other nonprotein substances, are not true anaphylaxis. This is also true of conditions resembling anaphylactic shock which are produced by proteins without previous sensitization, either natural or artificial.

Simpson showed that in primrose dermatitis it is not possible to sensitize an animal, either actively or passively, with the poison of the plant, and that the protein of the plant had nothing to do with causing the reaction. He concludes that the cases of skin eruptions caused by the primrose were instances of epithelial irritability and not dependent on any immunologic process.

45. Strickler and Goldberg: *J. A. M. A.* **66**:249, 1916.

46. Tracey: *Boston M. & S. J.* **175**:197, 1916.

47. Wodehouse and Olmsted: *Boston M. & S. J.* **176**:467, 1917; *J. Immunol.* **2**:3, 1917; *Boston M. & S. J.* **175**:195, 1916.

48. Ferry: *J. Lab. & Clin. M.* **2**:655, 1917.

49. Baker and Floyd: *Boston M. & S. J.* **175**:199, 1916.

50. Goodale: *Boston M. & S. J.* **179**:293, 1918.

51. Simpson: *J. A. M. A.* **69**:95, 1917.

52. Miller: *J. Path. & Bact.* **17**:249, 1913.

53. Richet: *Compt. rend Soc. de biol.*, 1898.

54. Thiels: *Ztschr. f. Immunitätsf. u. exper. Therap.* **16**:160, 1913.

The Intestinal Tract in Sensitization.—Talbot⁵⁵ finds that during infancy practically all cases of sensitization are due to foods. Because of adaptation or immunization, the idiosyncrasies to foods become less common as the age of puberty is reached. Asthma, recurrent bronchitis, eczema and gastro-intestinal indigestion are the diseases which are most commonly due to foods. This explanation, however, cannot be given as the cause in all cases of such diseases. Egg is the commonest offender in asthma cases, but some cases are sensitive to more than one food, especially in the case of cereal grains. Bacteria have been the cause in some cases. This author cites literature to show that the gastro-intestinal wall of new-born infants is permeable to undigested foreign protein. Soon the infant develops the power of destroying such proteins. Lust⁵⁶ and Hahn,⁵⁷ quoted by Talbot, showed that in a small percentage of babies with disturbances of digestion, precipitins to cow casein are demonstrable in the serum. There is evidence that in the case of egg and cow's milk, boiling reduces the liability to sensitization.

Schloss and Worthen⁵⁸ found that the intestinal tract of normal infants is usually impermeable to undigested foreign protein. In agreement with other authors quoted by them, they also found that in nutritional or gastro-enteric disorders, foreign protein may be absorbed in an undigested or partially undigested state and appear in the urine. From preliminary investigation they conclude that such foreign protein appears earliest in the blood but that it also appears in the urine and persists there for a longer time. In testing for such protein they used both anaphylactic tests and the precipitin reaction, finding that the latter was more delicate than the anaphylactic test which only became positive when there was enough protein in the urine to be coagulable.

Schlutz and Larsen⁵⁹ undertook the study of four types of diseases of the gastro-intestinal tract in children. These were extreme atrophy, overfeeding with cow's milk, periodic vomiting, and cases affected with the exudative diathesis, styled by Czerny, "inflammatory exudative diathesis." They obtained marked anaphylactic phenomena in animals which, sensitized by the serum of patients of the last group, were later injected with a small quantity of milk, usually intraperitoneally. Their results in the first three groups were not as definite as in the cases of exudative diathesis.

Greer,⁵⁹ by the intradermal injection of cow's milk in infants suffering from gastro-enteric disorders, agrees with these authors and

55. Talbot: Boston M. & S. J. **179**:1, 1918; **175**:409, 1916.

56. Lust: Jahrb. f. Kinderh. **77**:383, 1913.

57. Hahn. Jahrb. f. Kinderh. **77**:405, 1913.

58. Schlutz and Larsen: Arch. Pediat. **35**:705, 1918.

59. Greer: Arch. Pediat. **34**:810, 1917.

concludes that there is strong evidence of increased permeability of the intestinal wall to incompletely digested lactalbumin and to a lesser extent of caseinogen, and that sensitization takes place as a consequence.

Eczema.—Blackfan,⁶⁰ in forty-three persons who did not have eczema, found only one showing any evidence of susceptibility to protein, by cutaneous and intracutaneous tests. On the other hand, in twenty-seven persons having eczema, twenty-two showed susceptibility. This was usually to egg white, cow's milk, or human milk. With older children great improvement occurred in some cases if protein were withheld from the diet. In infantile eczemas this treatment is neither feasible nor successful. It is, in the first place, impossible to leave out animal protein from the infant's diet for a long interval without disturbing nutrition, and secondly, although such treatment might produce early improvement, the eczema shows a strong tendency to recur even while on the low protein diet.

White⁶¹ says that in the presence of eczema when neither fat nor starch is found in excess in the stools, one should look for hyper-susceptibility to egg albumin or to milk. In chronic eczema the great majority seems to exhibit sensitization to one or more food substances.

Walker⁶² reports cases in which the proteins of horse dandruff, ragweed, and timothy pollens may cause eczema, both from external exposure and internal injection in predisposed persons. Eczematous persons tolerate very small doses of the offending protein with improvement. This is a handicap in treating asthma in such patients because the amount of protein that benefits eczema is too small to prevent asthma, and the amount that immunizes against asthma makes the eczema worse. From these proteins, also, urticaria and angioneurotic edema were caused in some of their patients. McBride and Schorer⁶³ describe the erythematous and urticarial eruptions resulting from sensitization to certain foods.

Talbot⁵⁵ and Schloss⁶⁴ agree that immunization is practicable in the case of egg protein.

Hoobler⁶⁵ divides the symptoms of anaphylaxis in infancy into those relating to the skin, those of the upper respiratory tract, those involving the lower respiratory tract, those connected with the digestive organs, and those involving the nervous mechanism. He believes that many minor conditions may be due to protein sensitization and that proper food modification causes relief.

60. Blackfan: *Am. J. Dis. Child.* **11**:441, 1916.

61. White: *J. Cutan. Dis.* **34**:57, 1915.

62. Walker: *J. A. M. A.* **70**:897, 1918.

63. McBride and Schorer: *J. Cutan. Dis.* **34**:70, 1915.

64. Schloss: *Trans. Am. Pediat. Soc.*, 1915, p. 37.

65. Hoobler: *Am. J. Dis. Child.* **12**:129, 1916.

Respiratory Disturbances.—Asthma: Walker⁶⁶ believes that minor respiratory disturbances in many cases are the real beginning of later asthma and are the first symptoms of sensitization to some protein. In 400 patients it was found that first attacks were fairly evenly distributed among patients of different ages until the age of 45, when the primary cases became much less frequent. As the age of onset increases, the percentage of those who are sensitive to some protein diminishes. Succeeding ages of onset are accompanied by a gradual decrease in the number sensitive to animal hair proteins. Sensitization to food proteins was far more frequent in those persons who began their asthma during infancy, and, while at this age, eggs, milk, and cereals were most prominent among disturbing proteins, at later ages such proteins as fish, meat and potato became the more frequent. The frequency of sensitization to bacterial proteins was about the same for all ages up to 40. More were sensitive to the protein of *S. pyogenes aureus* than to any other bacterial protein.

Of the sixty-eight patients sensitive to food proteins, half were sensitive to the proteins of cereals, and wheat was by far the most common food to cause asthma. Next in order of frequency came egg, fish, potato and casein.

Asthma which occurs only during the summer months is usually caused by pollen proteins. In many instances this pollen asthma is prolonged throughout the year by bacteria which, because of the patient's lowered resistance, cause bronchitis and secondary asthma. A number of patients have asthma only in the early spring and late fall and associate their trouble with the changeable weather. In such cases bacteria are frequently the cause. Asthma of the winter months is usually bacterial. The longer the duration of the asthma, the more pronounced may be the resultant emphysema and the asthma may thus not be relieved without treatment of this condition.

Multiple sensitization is a great deal more common among those who began to have asthma during infancy. It is not very common among those having their first attack after the tenth year. A positive skin test with several different proteins may mean that only one or several are acting as the cause of the asthma. Treatment is largely a matter of judgment in deciding which positive test should be first investigated. If the patient is sensitive to food proteins, such foods should be omitted for at least a month in order to properly determine their effect. In the case of food proteins attempts to desensitize patients by the subcutaneous injection, or the gradual feeding of increasing amounts of the offending protein, have failed. Walker believes, how-

66. Walker: Boston M. & S. J. **179**:288, 1918; J. M. Res. **36**:231, 237, 423, 1917; **37**:310, 1917; J. A. M. A. **69**:363, 1917; Arch. Int. Med. **22**:466, 1918.

ever, that total abstinence for a long interval may desensitize patients. The results of dieting are most successful in cases of food sensitization.

Patients sensitive to bacterial proteins may be desensitized successfully by vaccine treatment. The first dose should not be larger than 100 million, and each succeeding dose should increase this by not more than one half this amount. Autogenous vaccine is preferable.

In treating patients who are sensitive to the proteins of horse dandruff or animal hair or pollens, the dosage should be guided by the dilution necessary to produce a skin reaction, 0.1 c.c. of the minimum dilution, increased at five or seven days intervals by additions of the same amount. Those sensitive to pollens should be treated in advance of the season. Occasionally it is necessary to use vaccines in conjunction with animal hair proteins in order to benefit the associated bronchitis. The permanency of relief depends on the amount of treatment and the patient's power of resistance.

In the case of nonsensitive patients by these skin tests, there is little to guide us. Occasionally, their serum agglutinates some type of organism and treatment with vaccines of that organism frequently benefits this asthma. Often they get relief or benefit through autogenous vaccines from the predominating bacterium of their sputum. The largest number have been relieved by vaccines of *Staphylococcus pyogenes aureus*, *Streptococcus hemolyticus* and diphtheroid organisms when these have predominated. Occasionally in those who are troubled more from catarrhal conditions of the nose and throat than from bronchitis, vaccines from these sources may be given. Naturally, the teeth and tonsils may be the seat of infection and should be put in satisfactory condition. Bronchial asthma must be kept distinct from cardiac and renal asthma. Walker⁶⁷ concludes that patients who have seasonal asthma caused by pollens are prevented from having asthma by a series of treatments with the pollens, provided sufficient treatment is given. The usual method employed by him consists in a series of injections of various dilutions of the pollen ranging from the strongest that fails to give a positive skin reaction to the strongest which gives a positive test. If a dilution of 1:10,000, give 0.2 c.c.; 1:5,000, give 0.2 c.c., 0.3 c.c., 0.4 c.c.; 1:1,000, give 0.2 c.c., 0.3 c.c.; 1:500, give 0.2 c.c., 0.3 c.c., 0.4 c.c.; 1:100, give 0.1 c.c., 0.2 c.c., 0.3 c.c.

Treatment during the season is less reliable but worth doing. In such cases very small amounts should be given. The continuation of asthma after the pollen season is due to secondary bacterial infection causing bronchitis in a patient whose resistance, either local or general, has been lowered because of prolonged severe pollen asthma.

67. Walker. Am. J. M. Sc. **157**:409, 1919.

The patients who have continuous asthma throughout the year should be treated with pollens if cutaneous tests are obtained with them.

The most common pollen that causes seasonal asthma is that of ragweed, whose pollen season extends, as a rule, from the middle of August to the first frost, or about the first of October. The next most common pollens are those of redtop and timothy, usually both together, but of the two, timothy is the most frequent. These, however, are poor seconds to ragweed pollen. Their season of pollination is June and July. Rarely, the various trees which pollinate during April and May, the pollen of the rose during June and July, the pollen of the daisy during July and August, and the pollens of corn and goldenrod during August and September, are the cause of asthma.

Babcock⁶⁸ lays stress on the removal of infectious foci from the mouth and the proper drainage of the nose before resorting to the immunization treatment of asthma.

Hay-fever.—This troublesome condition is most frequent in the late summer and early fall months, but may occur at other times of the year in different climates, depending on the susceptibility of an individual to various pollens. While bacteria may increase the intensity of the disease, or may cause a patient to become susceptible to it, hay-fever is probably always caused by pollens.⁶⁹ Cooke, Flood and Coca⁷⁰ conclude that hay-fever is the clinical symptomatic expression of local hypersensitiveness, the active pollen substances are not toxins. Secondly, that the hypersensitiveness is established spontaneously and never by immunologic process. This is shown in two ways, first that individuals may be sensitive to pollens of plants that are indigenous in foreign countries and with which they have never come in contact, and second, because individuals naturally sensitive to one protein only, cannot be artificially sensitized to another protein either animal or vegetable. They also consider that sensitization is not directly inherited, although the tendency to spontaneous sensitization is inherited as a dominant character. Fourthly, they conclude that the antibody substances of human sensitization are not demonstrable in the blood of sensitive persons by any of the immunity reactions. They are present in the cells of the sensitive tissues. Fifth, that the mechanism of the alleviating effect of specific therapy is the same as that of desensitization in experimental anaphylaxis.

Goodale⁵⁰ mentions the fact that the amount of pollen produced varies, depending on the season. Some hay-fever cases seem to him to be due to the fragrance alone, since the cause of the hay-fever in

68. Babcock: J. A. M. A. **68**:438, 1917.

69. Editorial, J. A. M. A. **70**:689, 1918.

70. Cooke, Flood and Coca: J. Immunol. **2**:217, 1917.

these instances are plants which, by nature, could disseminate only extremely slight quantities of pollen, and skin tests with the pollen are negative. A review of the true anaphylactic hay-fever cases seen by him during the previous four years shows that they may be divided into three main groups, namely: those occurring before the flowering of the grasses in April and June, and dependent on certain trees which disseminate large quantities of pollen, such as the maple, willow, birch and oak; second, the grasses in late May and throughout June; and third, by far the largest, in August and September, from ragweed.

Hall⁷¹ calls attention to the fact that west of the Rockies and in different parts of the world, hay-fever may be produced by an almost entirely different flora from that which causes it in the eastern states and Europe.

Sheppegrell⁷² has done some valuable work in cataloguing different hay-fever resorts in the United States and Canada. He has shown that the responsibility of the noxious plants for hay-fever depends first, on the proximity of these plants, and secondly, on the size of their pollen, which affects their buoyancy. For example, the pollen of corn is rarely responsible for hay-fever because of the large size of its pollen grains which limits the potential area of distribution to within a few yards of the plant. The ragweed pollen grain is one fifth the size of that of corn and has a buoyancy so great that a wind velocity of twenty miles will carry it several miles. Hay-fever resorts are valuable because they are free from certain pollens. Some give relief to one class of patients but not to others, therefore it is important to know not only the pollen to which a patient is sensitive, but also what pollens are found at the resort to which he is going. Ordinarily an altitude of 6,000 feet gives general protection, being free from most of the obnoxious plants. Any city which is kept entirely free from weeds will afford protection. Hay-fever resorts which are not by reason of altitude or climate, naturally protected against the growth of these plants are beginning to make regulations preventing the importation and transplantation of them.

Goodale⁷³ by injecting an alcoholic extract of coagulated pollen protein claims to be able to immunize more rapidly and with fewer doses than does Walker⁶⁶ with alkaline solutions of the protein. Frank and Strouse⁷⁴ believe that better results are obtained by combining early specific pollen immunization with late bacterial immunization.

Nonspecific Therapy.—There is a large and growing literature devoted to the treatment of various conditions by injecting foreign

71. Hall: Science **47**:516, 1918.

72. Sheppegrell: Pub. Health Rep., July 20, 1917, p. 1135, J. A. M. A. **71**: 523, 1918.

73. Frank and Strouse: J. A. M. A. **72**:1593, 1919.

protein of a nonspecific nature. The chief requisite seems to be that a sharp systemic reaction with fever and leukocytosis be produced. The initial rise in temperature may be followed by an abrupt decline to normal in pneumonia according to Cowie and Beaven.⁷⁴ Good results have been obtained in a variety of diseases and by a large number of observers, and their reports, in many instances, are so complete that there is no doubt that such therapy has proved its usefulness when used with proper knowledge and care. Miller and Lusk⁷⁵ and Cowie and Calhoun⁷⁶ report good results following the injection of such nonspecific proteins as albumose or typhoid bacilli in the treatment of arthritis. As with other observers, patients with acute cases were more favorably influenced than were chronic ones. It is doubtful if cardiac complications were improved. Gonorrheal patients also were improved. The severity of the reaction to the injection was less in patients with infections of low virulence, and thus it seems that the reaction is not entirely a matter of the protein introduced. These authors suggest that bacteria in the affected joints were destroyed and added to the reaction by liberating other foreign protein. This explanation would convey the impression either that there are fewer bacteria in chronic cases, or that such bacteria are less susceptible to the injection. Smith⁷⁷ reports success in eleven cases of gonorrheal arthritis by injecting normal horse serum instead of antigenococcus serum. In his cases the greater the reaction the better the result. In a later paper Miller⁷⁸ makes a similar statement, and says further that an injection not followed by a chill, although with marked leukocytosis, produces no beneficial results. The chief objection is the danger of grave or fatal reactions, and this form of therapy, according to this author, must be considered as being still in the experimental stage and may be placed in unwarranted disrepute by failure to observe proper precautions. Thomas,⁷⁹ after treating eighty-six patients who had subacute and chronic rheumatism, concludes that the relief of pain is not permanent in more than 30 per cent., but that the remaining patients have done much better than those previously treated and that such success and the small percentage of dangerous results must eventually force this method into more general use. Cowie and Beaven⁷⁴ state that, in pneumonia, the intravenous injection of protein is indicated only in the early stage, and is contraindicated in cases of influenzal pneumonia later than the third day. It is also contraindicated in cases showing undoubted

74. Cowie and Beaven: *J. A. M. A.* **72**:1117, 1919.

75. Miller and Lusk: *J. A. M. A.* **66**:1756, 1916; **67**:2010, 1916.

76. Cowie and Calhoun: *Arch. Int. Med.* **23**:69, 1919.

77. Smith: *J. A. M. A.* **61**:1758, 1913.

78. Miller: *J. A. M. A.* **69**:765, 1917.

79. Thomas: *J. A. M. A.* **69**:770, 1917.

evidence of advanced myocardial insufficiency or acute endocarditis. An intravenous injection of typhoid protein may bring about a termination of the acute symptoms in from one to three days. In the eleven cases of pneumonia quoted by these authors, it does not seem that more success was obtained than with the more recent specific intravenous treatment.

Auld,⁸⁰ following the work of Novy and DeKruif, claims good results in treating asthma with subcutaneous injections of a solution of Witte's peptone. This is accomplished by desensitization. As the injection is nonspecific there is no need of skin tests to determine the specific cause of the asthma. The desensitization is only temporary. His results were better in cases of recent onset with attacks at fairly regular intervals. Small and increasing doses except in special instances are more effective than large doses.

Investigating the mechanism of this therapy, Jobling and Petersen⁸¹ find that leukocytosis is not essential. Hyperpyrexia seems to be a factor, but the fundamental change seems to be that injections bring about a reduction of the state of colloidal dispersion affecting not only serum protein but also serum lipoids.

Danysz⁸² believes that certain symptoms in disease are the result of anaphylaxis induced by microbes, living or dead, or by some foreign albumin, incompletely digested. The resulting anaphylactic sensitization has to be overcome and the means for this do not need to be specific. He reports the treatment of 159 patients including 103 with various gastro-intestinal disturbances, with an antigen made from emulsifying the bacteria in the patient's stool, or a similar hetero-emulsion. Better results were obtained from the autoantigen. In the majority of cases benefit was immediately manifested.

Nolf⁸³ reports success with this form of treatment given intravenously in infectious diseases in Belgium. Specific vaccines, he considers more accurate, but both methods are of value. Shock is to be avoided but a mild reaction is advantageous.

Schamberg⁸⁴ reports uniform success in treating and immunizing against poisoning by ivy. He accomplishes this by the oral administration of small and increasing doses of the tincture of the plant. He suggests this method in immunizing against other proteins such as the pollens.

80. Auld: *Brit. M. J.* **1**:580, 749, 1917; **2**:49, 1918.

81. Jobling and Petersen: *J. A. M. A.* **66**:1753, 1916.

82. Danysz: *Presse méd.* **26**:307, 1918; *Paris méd.* **9**:3, 1918.

83. Nolf: *J. A. M. A.* **72**:1901, 1919.

84. Schamberg: *J. A. M. A.* **73**:1213, 1919.

Vernoni⁸⁵ considers that the liability to anaphylactic shock is much diminished by intraspinal injections of foreign serum instead of the usual intravenous or subcutaneous injections. The exceptions to this are cases in which there is inflammation of the meninges. Lewis⁸⁶ suggests that the slow injection of foreign serum will prevent serum sickness in many cases.⁸⁷

85. Vernoni: *Riv. di Clin. Pediat.* **2**:337, 1917.

86. Lewis: *J. A. M. A.* **72**:329, 1919.

87. Weil: *J. Immunol.* **2**:95, 1916. Hemple: *J. Immunol.* **2**:157, 1916. Smith and Cook: *J. Immunol.* **2**:269, 1917; **3**:35, 1917. Wells and Osborne: *J. Infect. Dis.* **17**:259, 1915. Davis: *J. A. M. A.* **68**:159 (Jan. 20) 1917. Rackemann: *Arch. Int. Med.* **22**:517 (Oct.) 1918.

The American Medical Association will pay thirty cents each for the following issues of the *AMERICAN JOURNAL OF DISEASES OF CHILDREN*: January, 1913; February, March, November and December, 1914; January and August, 1915; January, 1918; March and April, 1919. Address to AMERICAN MEDICAL ASSOCIATION, 535 North Dearborn Street, Chicago, Ill.

THE EFFECT OF INTRAVENOUS INJECTIONS OF CALCIUM IN TETANY AND THE INFLUENCE OF COD LIVER OIL AND PHOSPHORUS IN THE RETENTION OF CALCIUM IN THE BLOOD*

ALAN BROWN, M.B.; IDA F. MacLACHLAN, B.A.,

AND

ROY SIMPSON, M.B.

TORONTO

Most observers who have written on the subject of infantile tetany connect the cause with a disturbance of the calcium metabolism, the greater number believing it to be due to a deficiency of calcium in the tissues. The intimate association of rickets and tetany, in the former of which there is a definite disturbance of calcium, has been sufficient to suggest to many that the same salt is probably instrumental in the causation of tetany. The favorable influence of calcium on tetany, which will be discussed subsequently, gives weight to the view that a deficiency of calcium may play a part in the production of tetany.

Kassowitz¹ and his adherents have insisted that tetany is just a symptom of rickets. From extensive clinical, and a few metabolism, observations, we are inclined to regard this statement as correct. We have not yet seen a case of tetany that did not show some clinical signs of rickets. Our observations do not coincide with Howland and Marriott's to the effect that tetany is found occasionally in infants who present no signs of rickets.

There is still considerable diversity of opinion regarding the therapeutic employment of calcium, and not sufficient use made of the most effective remedy, cod liver oil and phosphorus. It was after a consideration of these two points, combined with the statement made by Howland and Marriott² that calcium given by mouth has a very prompt effect in preventing all of the symptoms of active tetany, that we were prompted to undertake this investigation.

* From the wards and laboratories of the Hospital for Sick Children, and the Department of Pediatrics, University of Toronto.

1. Kassowitz: *Jahrb. f. Kinderh.* **75**:2 (Feb.) 1912.

2. Howland and Marriott: *Quart. J. Med.* **11**:289 (July) 1918.

Stoeltzner³ and his co-workers believe there is a stagnation of calcium in the tissue. Cybulski⁴ and Schabad⁵ are convinced that the calcium excretion is not regularly increased in tetany, yet the latter finds that on giving cod liver oil and phosphorus, there is a gradual reduction of electrical irritability with the simultaneously increased calcium retention. Schwarz and Bass⁶ failed to find any lessening of calcium retention. McCallum and Voegtlin⁷ observed that in parathyroidectomized dogs the injection of calcium and magnesium salts stops all symptoms of tetany, and that the injection of sodium and potassium salts has the opposite tendency. In addition to this, they found a reduction of the calcium content of the tissues and blood during tetany, and increased excretion of calcium in the urine and feces while the tetany is developing. Rosenstern⁸ reduced the electrical irritability by giving calcium in large amounts by mouth.

Zybell⁹ concluded that experimental results showed no agreement as to the effect on infants suffering from tetany, of long continued feeding of small or large doses of calcium, although occasionally one finds a slight reduction in the electrical irritability in the employment of large doses of this salt. He does not believe in any specific salt therapy.

The influence of calcium on the symptoms of tetany has been studied in two ways. The first method was employed in an endeavor to disprove Stoeltzner's hypothesis. Bogen,¹⁰ Risel,¹¹ Rosenstern,⁸ Zybell,⁹ and others, administered calcium in various forms and doses; they usually employed but one dose and determined its effect on the electrical reactions. From this single effect only a temporary reduction of the symptoms was observed.

Netter¹² and Goppert,¹³ on the other hand, have consistently used calcium in repeated doses, and have noted only an alleviation of the clinical symptoms, no observations being made on the electrical or other signs of tetany. Recently, Howland and Marriott conducted an interesting series of observations on the calcium content of the blood in tetany. These observers conclude without reservation, that calcium has a very prompt effect in preventing all of the symptoms of active tetany. They emphasize the fact that calcium administra-

3. Stoeltzner: *Jahr. f. Kinderh.* **12**:661, 1916.

4. Cybulski: *Monatschr. f. Kinderh.* **5**:409, 1906.

5. Schabad: *Monatschr. f. Kinderh.* **9**:25, 1910.

6. Schwarz and Bass: *Am. J. Dis. Child.* **1**:15, 1912.

7. Macallum and Voegtlin: *J. Exper. Med.* **11**:118, 1909.

8. Rosenstern: *Jahrb. f. Kinderh.* **72**:154, 1912.

9. Zybell: *Jahrb. f. Kinderh.* **77**:29, 1913.

10. Bogen: *Monatschr. f. Kinderh.* **6**:228, 1907.

11. Risel: *Arch. f. Kinderh.* **72**:154, 1910.

12. Netter: *Compt. rend. Soc. de biol.* **62**:376, 1907.

13. Goppert: *Med. Klin., Berlin*, **10**:1003, 1914.

tion must be continued, however, for a long time; in addition to this, they also found that in tetany, during the active symptoms, the calcium of the serum invariably is greatly reduced and may fall as low as 3.5 mg., while the average was 5.6 mg. They stated further, that in rickets the calcium shows only a moderate reduction, in some instances to 8 mg.; but in a number of their apparently active cases a normal amount of calcium was present.

To date there have been no recorded observations on the influence of intravenous injections of calcium and the effect on the retention of calcium in the blood, and consequent reduction of symptoms. The nearest approach to our observations is that of Maggiore¹⁴ who injected calcium chlorid intravenously in 1, 2, 3 or 5 c.c. doses. He observed that the effect was most pronounced by the third injection and began to decline by the twelfth hour. A similar effect was observed following the second injection, but no observations are recorded in reference to the blood calcium, nor is it noted whether or not the infants were cured. Severe reactions were recorded.

Our observations were conducted on fourteen cases of frank tetany, all of which showed varying degrees of rickets. Our studies were divided in the following way:

1. Normal blood calcium on eighteen infants under 1 year of age.
2. The effect of intravenous injections of calcium lactate on blood calcium, and on the symptoms.
3. The effect of codliver oil and phosphorus on the blood calcium and the clinical result.

METHODS OF OBSERVATION

A diagnosis of tetany depended on the presence of one or other of the following signs: Chvostek, Trousseau, carpopedal spasm, laryngeal spasm, and convulsions. The degree of intensity of each particular sign was denoted by ++ or ++++, etc. In this matter a fair degree of accuracy was obtained. The electrical tests were made with a galvanic, dry cell battery equipped with a switch for reversing polarity, a rheostat for controlling the strength of current, and a balanced milliamperimeter measuring from 0.2 to 10 milliamperes. In every instance the peroneal nerve-muscle group was employed, the negative electrode being placed over the abdomen, and the positive electrode over the peroneal nerve as it winds around the head of the fibula.

The technic for blood calcium employed was that recommended by Lyman.¹⁵ No changes were made in the method. The blood in every instance was removed from the longitudinal sinus, and the calcium

14. Maggiore: *Pediatrics* **27**:129 (March) 1919.

15. Lyman: *J. Biol. Chem.* **29**:169 (March) 1917.

was estimated on the whole blood and not on the blood serum, because the red blood corpuscles contain calcium, although in a somewhat smaller concentration than the serum (Cowie¹⁶).

The readings were made on a Kober's nephelometer-colorimeter. For each determination an average of six readings was taken. The results by this method are accurate to within less than 1 per cent.

The Calcium of the Blood in Infants Under Normal Conditions Under 1 Year of Age.—It is apparent that merely from the determination of the intake and excretion of calcium little can be learned. It is of prime importance to determine the quantity of calcium circulating in the blood. With the usual methods of analysis this has been impossible, unless from 50 to 100 c.c. were withdrawn, with double the amount if duplicate determinations were made, thus making it an impossible procedure in living infants. As a result, however, of the development of Lyman's method, it has been made possible to estimate the calcium on 5 c.c. of blood with, as mentioned previously, an error of 1 per cent. Howland and Marriott's¹⁷ method requires 2 c.c. of serum, is more complicated, and has an error of not more than 5 per cent.

The cases for the determination of normal blood calcium were selected from infants under 1 year of age, who showed no signs of rickets or any mechanical or electrical evidence of tetany. The lowest calcium content was found to be 8.2 mg. per hundred c.c. of blood, and the highest 11.1 mg. The average of all the determinations was 9.5 mg. for infants under 1 year of age.

TABLE 1.—GROUP A. INFANTS FROM 1 TO 3 MONTHS OF AGE

Name	Mg. of Ca. per 100 c.c. Blood
W. B. H.....	9.3
H. B. H.....	10.5
B. B. H.....	9.1
S. B. H.....	9.9
J. R.	10.8
T. McD.	10.0
B. D.	11.1
Average	10.1

TABLE 2.—GROUP B. INFANTS FROM 3 TO 6 MONTHS OF AGE

Name	Mg. of Ca. per 100 c.c. Blood
M. M.	8.2
F. S.	8.2
H. F.	8.3
J. C.	10.0
E. M.	10.3
Average	9.0

16. Cowie and Calhoun: J. Biol. Chem. **37**:505 (April) 1919.

17. Marriott and Howland: J. Biol. Chem. **32**:233, 1917.

TABLE 3.—GROUP C. INFANTS FROM 6 TO 12 MONTHS OF AGE

Name	Mg. of Ca. per 100 c.c. Blood
N. F.	8.2
E. N.	9.2
H. B.	9.2
L.	10.0
D.	9.2
B.	10.2
Average	9.3
Average calcium content under 1 year.....	9.5 mg.

Effect of Intravenous Injections of Calcium Lactate on Blood Calcium, and Its Effect on the Symptoms.—In conducting these observations an endeavor was made to keep the infants on the same type of food throughout the period; i. e., a plain milk and water mixture with enough sugar added to meet caloric requirement, with the mixture brought to the boil. In certain cases, however, protein milk was used where the stools were too loose or frequent to warrant the use of a milk and water mixture.

REPORT OF CASES

CASE 1.—A. B., age 9 months; white; admitted March 21, 1919; discharged April 22, 1919; cured. Brought to hospital on account of failure to gain weight, and constipation. Previous feeding history: Condensed milk and Allenbury's food, for a period of two months, followed by various milk and water mixtures with rusks.

Physical Examination.—Weight 12½ pounds. Definite Trousseau, Chvostek and carpopedal spasm. Pronounced craniotabes and some enlargement of the epiphyses.

Treatment.—On admission he was given cod liver oil and phosphorus, 10 minims, three times daily, gradually increased to 30 minims, three times daily. This was continued throughout his stay in the hospital. For seventeen days, from March 21 to April 7, during which time he had been having cod liver oil and phosphorus, there was no change in the electrical irritability. April 7, 1.25 gm. calcium lactate was given intravenously, with no untoward reaction at the time of injection. Following this the child was drowsy and pale for seven hours, with complete absence of all signs of tetany. In five days following the injection the electrical irritability had reached a normal point. The blood calcium had increased from 5.9 mg. per hundred c.c. of blood to 9.3 mg. During this interval all the mechanical signs had disappeared (Figs. 1 and 2).

CASE 2.—M. G., age 5 months; white; admitted March 28, 1919, discharged April 29, 1919; cured. Brought to hospital on account of convulsions and vomiting for seven days, and constipation since birth.

Previous Feeding History.—Breast fed for five weeks; milk and water mixture for two weeks, and then condensed milk till admission.

Physical Examination.—Weight 10½ pounds. Definite Chvostek, No Trousseau and no carpopedal spasm. Showed some craniotabes and bossing, with epiphyseal enlargement.

Treatment.—April 1, 1919, child was given cod liver oil and phosphorus, 15 minims, three times daily, gradually increased to 20 minims, three times daily. This was continued throughout the child's stay in the hospital.

For seven days, while on cod liver oil and phosphorus, there was a gradual increase in electrical irritability. On one estimation during this period the

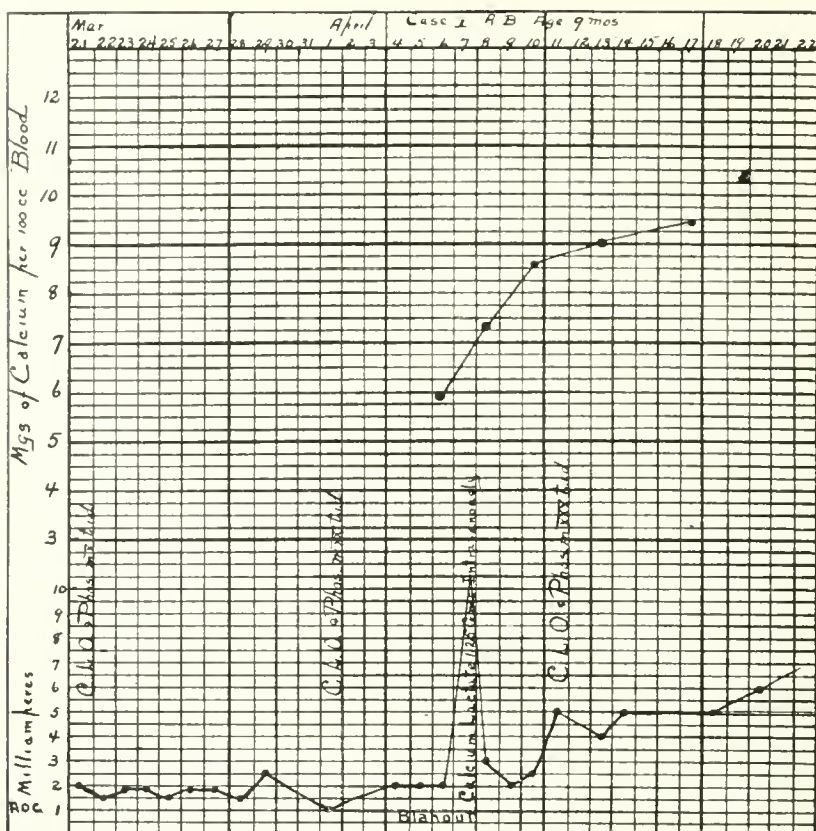


Fig. 1.—Shows the gradual reduction (lower line) in Case 1 in the electrical irritability under the influence of cod liver oil and phosphorus. The upper line shows the gradual increase in blood calcium.

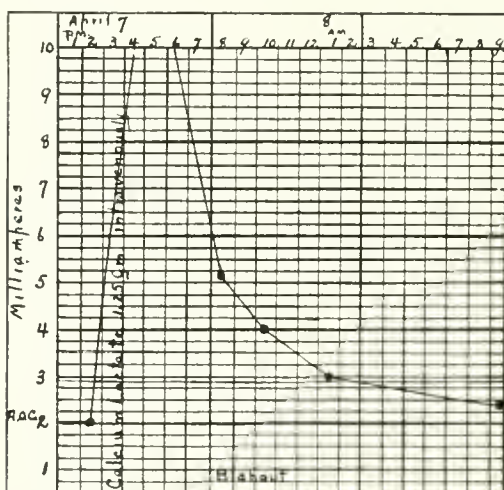


Fig. 2.—The two hourly electrical reaction (AOC) following an intravenous injection of 1.25 gm. calcium lactate.

blood calcium was 5.9 mg. April 7 calcium lactate was given intravenously. This was followed in a few minutes by complete collapse, which lasted about half an hour, and was succeeded by a period of drowsiness lasting four hours, with absence of electrical and mechanical signs for eight hours. For four days succeeding the injection, the electrical irritability was approximately the same as before, then it gradually began to decrease until the patient was discharged. The blood calcium gradually increased from the time of injection up to 7.8 mg., at which point observations were stopped (Fig. 3).

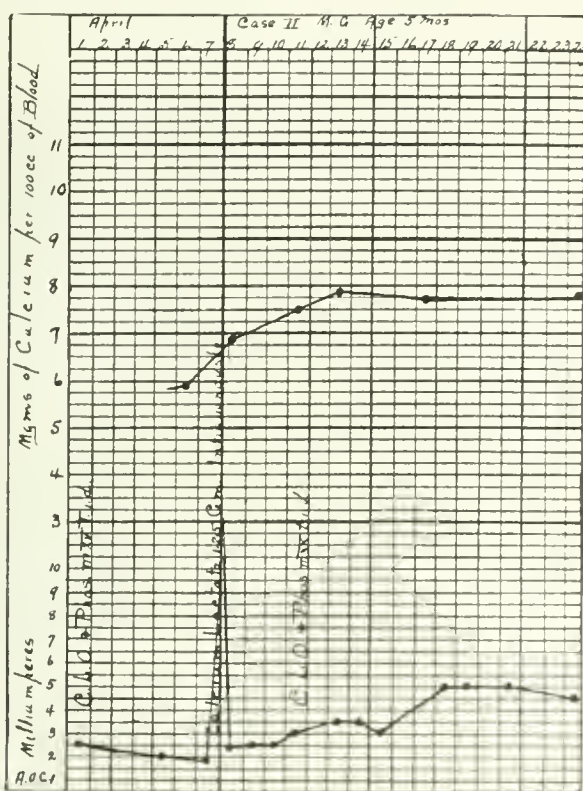


Fig. 3 (Case 2).—Findings as in Case 1 (Fig. 1).

CASE 3.—A. Q., age 8 months; white; admitted April 3, 1919; discharged May 21, 1919; cured. Brought to hospital on account of convulsions of one week duration, and crowing noise while crying, for three weeks.

Previous Feeding History.—Breast fed for three weeks; patent foods for seven weeks; boiled milk, water and sugar mixtures until admission.

Physical Examination.—Weight 10½ pounds. Marked Chvostek, Trousseau, laryngeal spasm and carpedal spasm. Definite craniotabes and some epiphyseal enlargement.

Treatment.—Castor oil was given. In this case no medication specific for tetany was given for four days, during which time the electrical and mechanical irritability remained stationary. The blood calcium was 6.4 mg. per hundred c.c. of blood. April 7 calcium lactate was given intravenously; this was followed by a period of dyspnea, and cyanosis lasting one hour. For ten hours there wa

no electrical irritability, and no mechanical signs, but eighteen hours after injection, both of these were as marked as before. For the subsequent five days the electrical and mechanical signs were the same as before the injection. The blood calcium remained unaltered.

April 14, calcium lactate was again given intravenously, followed by a period of coughing, lasting one hour, slight cyanosis, dyspnea succeeded by marked pallor and drowsiness which lasted two hours. No abnormal electrical irritability was elicited for eight hours. The decrease in electrical irritability was less marked than after the previous injection, but four hours after the injection a very slight laryngospasm was noticed. In thirteen hours all the mechanical and electrical signs had returned.

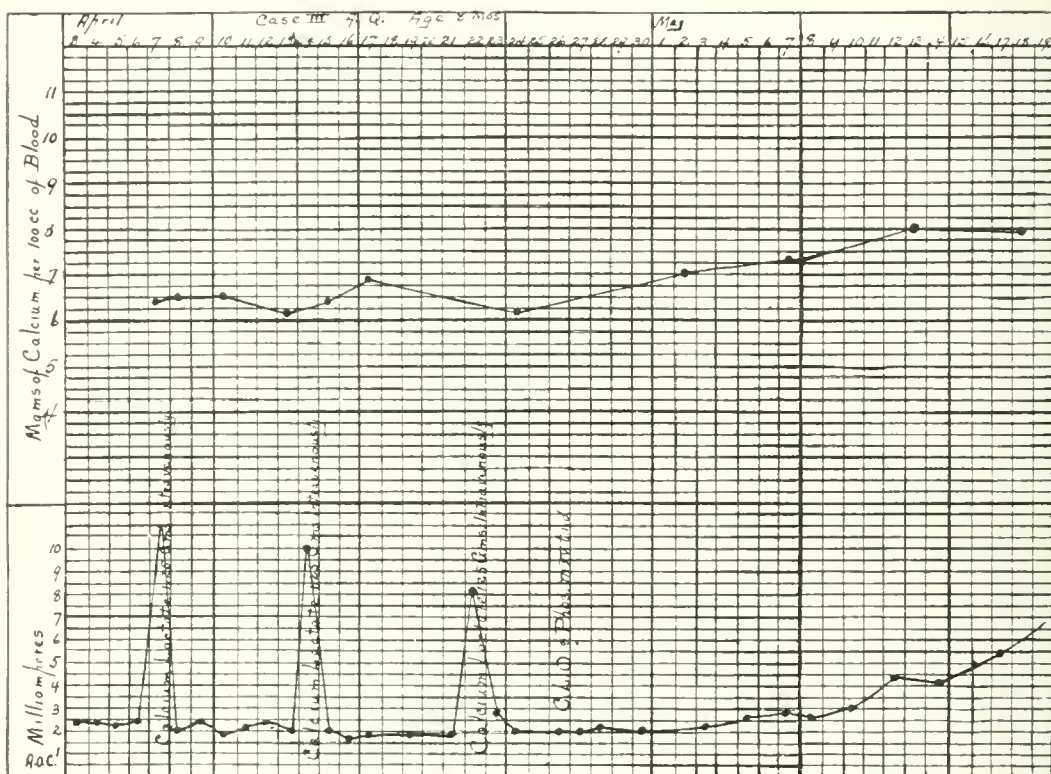


Fig. 4 (Case 3).—Effect on the electrical reactions of three successive doses of calcium lactate given intravenously (lower line). No change occurred in electrical reactions till cod liver oil and phosphorus were added. The upper curve represents the blood calcium which is seen to increase shortly after the administration of cod liver oil and phosphorus.

For six days following this second injection the electrical irritability and mechanical signs were more marked than ever before. Calcium content of blood showed only a very slight change, viz., 6.8 mg. per hundred c.c. of blood.

A third intravenous injection of calcium was given April 22, followed by only a very transitory attack of coughing with a tenacious mucus secretion. A marked decrease (not so much as after either previous injections) was observed in the electrical irritability, lasting six hours, accompanied by absence of mechanical signs for two hours. In sixteen hours all the signs were as

accentuated as before the injection. Three days after this last injection, April 26, during which time the electrical and mechanical signs and the blood calcium remained as before, cod liver oil and phosphorus, 15 minims, three times daily, was begun, gradually increasing to 20 minims, three times daily. Seven days following this there was no definite change in any way. Subsequently, however, the electrical irritability and mechanical signs gradually became less pronounced, until about May 10, when both had disappeared. The blood calcium had increased during this last period to 8.0 mg. (Fig. 4).

CASE 4.—O. C., age 10½ months; white; admitted April 1, 1919; discharged May 13, 1919; cured. Brought to hospital on account of cough for one month, and fever for two days, no convulsions.

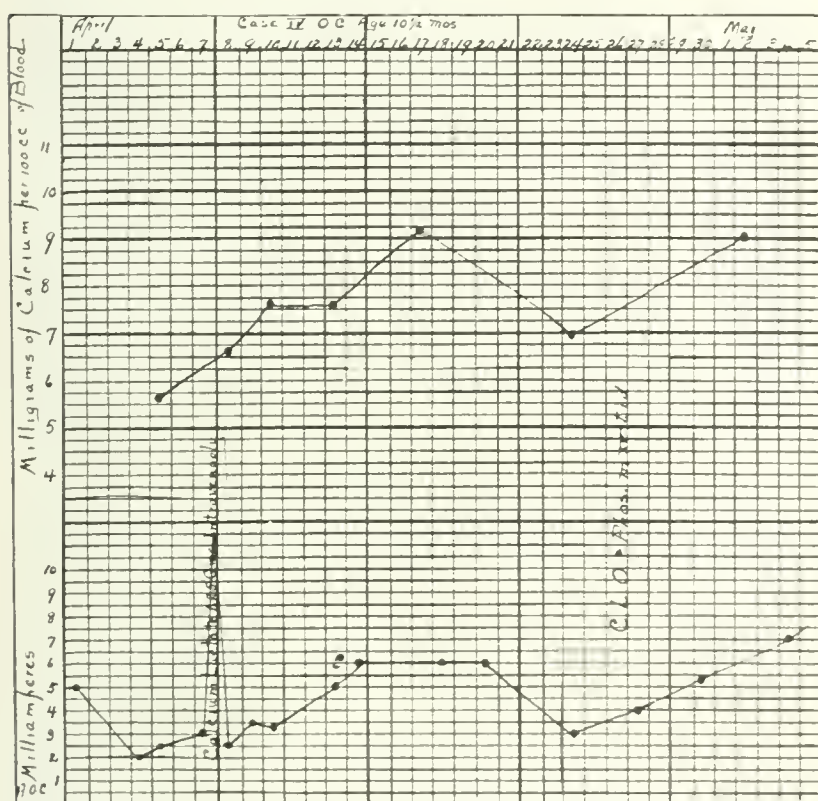


Fig. 5 (Case 4).—At first there was a gradual increase in calcium in the blood coincidentally with a gradual decrease in electrical irritability. Cod liver oil and phosphorus were not given till definite electrical and blood calcium changes had occurred.

Previous Feeding History.—Breast fed for four months, and milk and water mixture until the present.

Physical Examination.—Weight 12¼ pounds. Marked Chvostek; no Trouseau or carpopedal spasm; slight cramples, definite parietal and frontal bossing, with some epiphyseal enlargement.

Treatment.—On admission, April 3, the child was given protein milk, barley water and dextri-maltose with 1 gm. urea daily.

For the first six days' stay in the hospital, during which time she was getting urea and protein milk, the electrical irritability was markedly increased. The blood calcium was 5.7 mg. per hundred c.c. On the seventh day of the treatment, April 7, calcium lactate was given intravenously with no undesirable reaction. It was followed, however, by a period of drowsiness, lasting only three hours, and a period of ten hours in which all mechanical irritability was very much reduced, during eight hours of which all mechanical signs had disappeared. In eighteen hours all signs of tetany had returned. April 9, the urea was discontinued. Six days following the injection, the electrical and mechanical irritability gradually decreased. The blood calcium increased to the normal limit. For the subsequent week there was no change, when suddenly the calcium decreased, the electrical irritability increased and the previous mechanical signs reappeared. This lasted for two days only, when during the next seven days all signs disappeared and the calcium again returned to normal. We found no satisfactory explanation for this rather unexpected turn of events. It seems reasonable to assume, however, in view of the work of one of us on tetany, that the cure in this instance was effected by the high protein diet producing a favorable diuresis. April 26, cod liver oil and phosphorus, 15 minims, three times daily, was begun and continued until child was discharged (Fig. 5).

DISCUSSION

In each one of these four cases there was a distinct reaction after the intravenous injection of 1.25 gm. of calcium lactate. The degree of reaction varied from slight drowsiness to almost complete collapse, accompanied by dyspnea and some cyanosis, and in one instance pallor. These signs of reaction disappeared any time between one and seven hours; the more severe the reaction the longer the infant took to recover.

In each instance there was a temporary absence of both mechanical and electrical signs of tetany varying from seven to ten hours, after which period they rapidly returned to where they were before the injection.

In every case throughout the period of observation there was a distinct increase in the blood calcium; the lowest being 5.7 mg. before treatment and 9.3 after treatment. Whether the increase in each case was due to the retained calcium after injection, it is impossible to state, as other factors have to be considered. In Cases 1 and 2, undoubtedly cod liver oil and phosphorus played some part in binding or holding the injected calcium in the blood, as in both instances the drug had been given over a period of from two and a half to one week, respectively, before the injections were given; at any rate, it appeared to us that the blood calcium was retained more rapidly with intravenous calcium than with cod liver oil and phosphorus alone.

In Cases 1 and 2 there was a distinct increase in the blood calcium within forty-eight hours. Coincidental with the increased retention of calcium in the first two cases, we found the electrical irritability reduced and the mechanical signs of tetany gone.

In Case 3 three successive intravenous injections of calcium were made with varying degrees of reaction. No definite change, however, was observed (other than temporary, following injections) in either the blood calcium or electrical reactions until cod liver oil and phosphorus had been employed for a period of ten days. Whether this bore any relation to the changes observed, of course, it is impossible to state positively. It is, however, suggestive, that the cod liver oil and phosphorus held the calcium in the system for these two weeks, and after this addition, the mechanical and electrical signs disappeared. No changes had been observed in the three weeks previous to the cod liver oil and phosphorus addition in spite of the intravenous injections of calcium.

In Case 4 we have no other explanation for the rather unexpected turn of events than that the high protein diet combined with urea produced a favorable diuresis, in this manner eliminating the sodium and potassium salts and reducing the irritability. We do not feel that the single injection of calcium exerted any influence on the child's condition, beyond, of course, the expected temporary reaction; certainly the addition of cod liver oil and phosphorus had no effect, as changes too definite to be ignored had already occurred before its addition.

Effect of Cod Liver Oil and Phosphorus on the Blood Calcium and Reduction of Symptoms.—Five cases were studied to determine this result.

REPORT OF CASES

CASE 5.—R. H., age 7 months; white; admitted April 4, 1919; discharged May 5, 1919; cured. Brought to hospital on account of convulsions, and holding breath spasm off and on for the past six weeks.

Previous Feeding History.—Breast fed for four months. Until admission has had unboiled milk and water mixture with sugar.

Physical Examination.—Weight 16½ pounds. Laryngospasm present. No Chvostek or Trousseau, no carpopedal spasm on admission (these were all elicited on the following day). Definite craniotabes and some enlargement of the epiphyses was noted.

Treatment.—Three days after admission, the child was given cod liver oil and phosphorus, 20 minims, three times daily, which was continued throughout her stay in the hospital. For three days after admission this child was given no antitetanoid medication, except castor oil on night of admission. During this time there was no change in any of the signs. Calcium in whole blood was 7.5 mg. per hundred c.c. April 7, cod liver oil and phosphorus, 20 minims, three times daily was given. For a period of thirteen days after this there was no change in the signs nor in the calcium content of the blood; but during the subsequent twelve days there was a gradual, but marked, decrease in the electrical irritability, disappearance of mechanical signs, and return of the calcium content of the blood to normal. No calcium lactate was given (Fig. 6).

CASE 6.—G. L., age 11 months; white; admitted March 30, 1919; discharged May 2, 1919; cured. Brought to hospital on account of five convulsions, and choking spells during past month.

Previous Feeding History.—Breast fed for three months, and malted milk from then on until admission.

Physical Examination.—Weight 19¾ pounds. Definite Chvostek, Trousseau and laryngospasm. No carpopedal spasm. Distinct craniotabes and slight epiphyseal enlargement.

Treatment.—On admission the child was given castor oil and fed protein milk with urea, 1 gm., in day's feedings. This feeding was continued for two days, when the protein and urea was discontinued, and a boiled milk and water

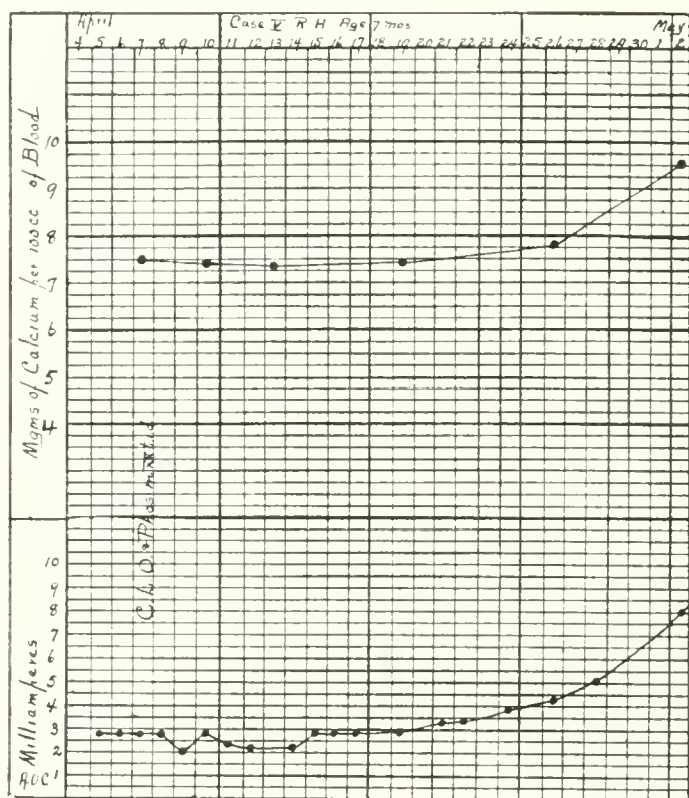


Fig. 6 (Case 5.)—Gradual reduction in electrical irritability coincidently with a gradual increase in blood calcium after the administration of cod liver oil and phosphorus.

mixture was given. This was continued for seven days, during which time the electrical and mechanical irritability increased.

The calcium content of the blood was then 7.2 mg. April 7, he was again given protein milk and urea, and in two days more cod liver oil and phosphorus, 20 minims, three times daily, was given, and this was increased to 30 minims, three times daily, in four days. During this time there was no change in the signs or calcium content of the blood. At this time the child contracted a parenteral infection, and during the next seven days had a fever during which time the electrical irritability was decreased, while the mechanical signs and

the calcium content of the blood were practically unchanged. During the next week the mechanical signs had for the most part disappeared, and the calcium content of the blood increased to within the normal limit (Fig. 7).

CASE 7.—T. H., age 6 months; white; admitted April 3, 1919; discharged April 27, 1919; cured. Brought to hospital because of five convulsions one month previous, and constipation.

Previous Feeding History.—Breast fed for three weeks; then milk and water mixture for four months, followed by condensed milk until time of admission.

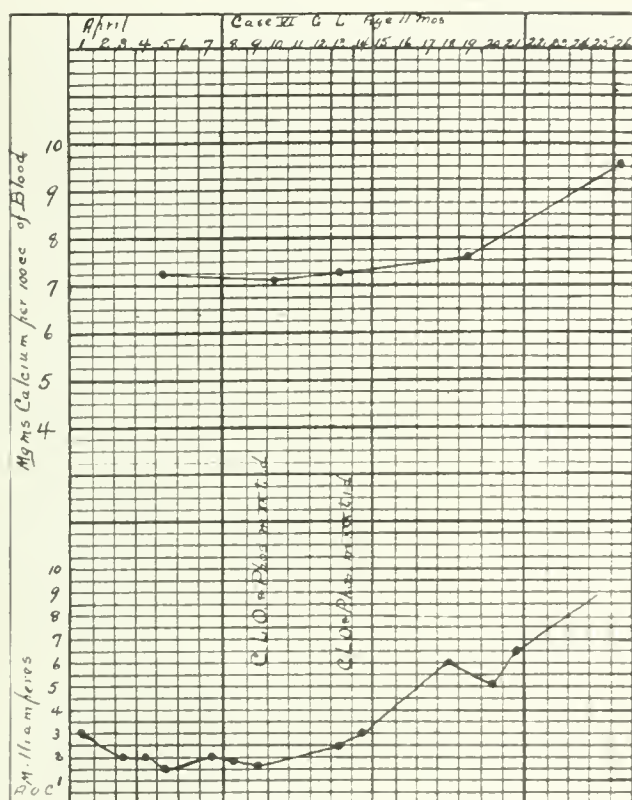


Fig. 7 (Case 6).—Findings same as in Case 5 (Fig. 6).

Physical Examination.—Weight 14½ pounds. Slight craniotabes and cephalic enlargement. Definite Trousseau and Chvostek; no laryngospasm.

Treatment.—Six days after the child was admitted, he was given cod liver oil and phosphorus, 20 minims, three times daily, on which he remained until discharged. During these six days he had a boiled feeding, and no medication; during this period there was no change in the signs of tetany; blood calcium was 6.6 mg. per hundred c.c. For the next seven days after the above period there was no change.

Following this, and until discharge, there was a gradual decrease in electrical irritability and disappearance of mechanical signs, and a gradual increase in calcium content of the blood to 8 mg. per hundred c.c. blood (Fig. 8).

CASE 8.—T. C., age 7½ months; Italian; admitted April 10, 1919; discharged May 10, 1919; cured. Brought to hospital because of convulsions every half hour for the previous twelve hours.

Previous Feeding History.—Always breast fed, with some cereal for the past two weeks.

Physical Examination.—Weight 13½ pounds. Very marked craniotabes, frontal and parietal bosses, and epiphyseal enlargement. Definite Chvostek, Trousseau, carpopedal spasm and laryngospasm.

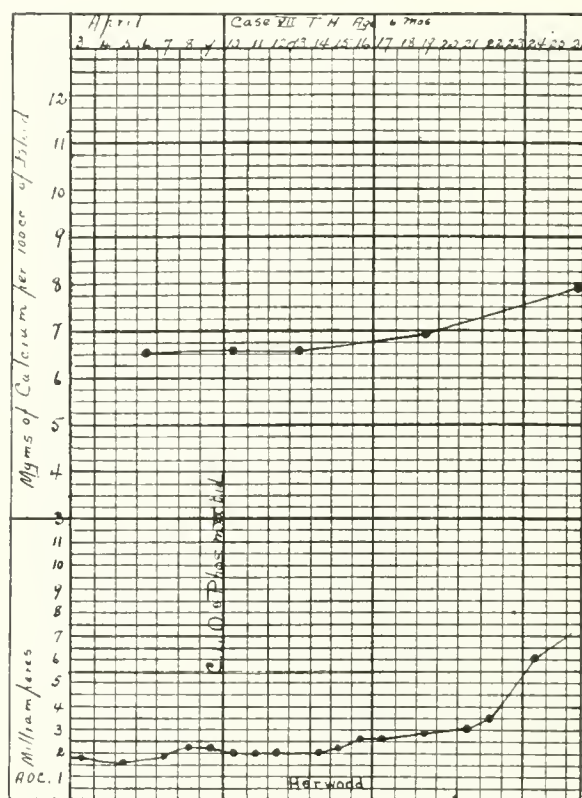
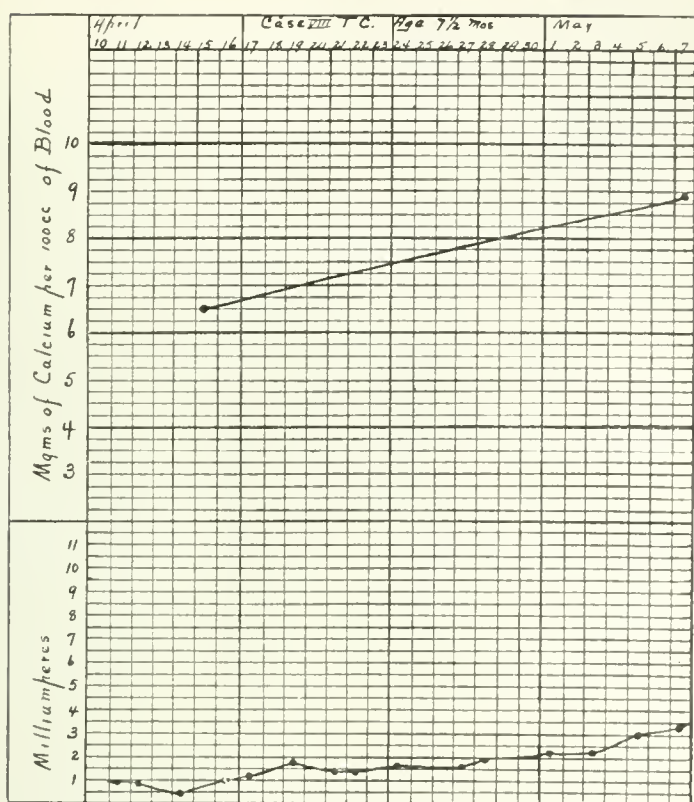


Fig. 8 (Case 7).—Findings same as in Case 5 (Fig. 6).

Treatment.—On admission she was given protein milk and urea, 1 gm., daily; cod liver oil and phosphorus, 20 minims, three times daily, gradually increased to 30 minims, three times daily, on which treatment she remained throughout her stay in the hospital. Electrical irritability disappeared at the end of three weeks. April 15, blood calcium was 6.5 mg. and May 7 it was 8.9 mg. (Fig. 9).

CASE 9.—W. M., age 8½ months; white; admitted March 21, 1919; discharged April 10, 1919; cured. Brought to hospital with a history of several convulsions during the past six weeks.

Previous Feeding History.—For one and one half months he was breast fed, after this, and until admission, he was fed McKay's patent barley with condensed milk.



Physical Examination.—Weight 14½ pounds.* Definite craniotabes and pronounced epiphyseal enlargement. There was definite laryngospasm, carpopedal spasm with very pronounced Chvostek's and Trousseau's signs.

Treatment.—During the first ten days after admission, the child was given a protein feeding with 1 gm. urea in each twenty-four hours. Castor oil was given for one dose only. He was started at once on cod liver oil and phosphorus, 20 minims, three times daily. At the end of this period he was given a milk and water feeding with no urea. During this period there was a very slight change in the electrical irritability or mechanical signs; the calcium content of the blood was not followed. On the twelfth day after admission, cod liver oil and phosphorus was increased to 30 minims, three times daily, and during the next eight days there was a definite decrease in electrical irritability and gradual disappearance of mechanical signs (Fig. 10).

In each of these cases, except Case 9, in which calcium was not estimated, there was a gradual increase in the blood calcium which coincided fairly accurately with the reduction in the electrical irritability. From our observation of these cases and many others we expect a reduction in the symptoms of tetany about ten days to two weeks following the administration of cod liver oil and phosphorus. This electrical reduction, as is seen in the charts, agrees rather well with the increase in the blood calcium. Case 9 graphically shows a gradual reduction of electrical reaction under the influence of cod liver oil and phosphorus. No blood calcium was estimated in this instance.

CONCLUSIONS

1. Constitutional reactions are produced following intravenous injection of calcium lactate in 1.25 gm. doses. The degree of reaction varied from a slight drowsiness to almost complete collapse accompanied by dyspnea. The signs of reaction disappeared usually between one and seven hours; the more severe the reaction the longer it took the patient to recover.

2. Intravenous injection of calcium lactate in 1.25 gm. doses produces a temporary absence of both electrical and mechanical signs of tetany usually lasting from seven to ten hours.

3. Calcium lactate injected intravenously, apparently exerts no beneficial therapeutic effect unless supplemented by the administration of cod liver oil and phosphorus, and in this instance the reduction of the tetanoid symptoms is a little more rapid than with the employment of cod liver oil and phosphorus alone.

4. Cod liver oil and phosphorus produces an increase in the blood calcium with a corresponding reduction in the mechanical and electrical signs, within a period of from ten to seventeen days.

THE NITROGENOUS AND SUGAR CONTENT OF THE BLOOD OF THE NEW-BORN

J. P. SEDGWICK, B.S., M.D.

Professor and Chief of the Department of Pediatrics

AND

MILDRED R. ZIEGLER, M.S.

Instructor in Pediatrics, University of Minnesota

MINNEAPOLIS

The chemistry of the blood of the normal new-born has been studied in only a few cases, largely because of the difficulty of obtaining blood in sufficient amounts for the analysis of more than one constituent. Howland and Marriot¹ have shown that the values for calcium are essentially the same as those found in the adult. Pettibone and Schultz² have made similar observations on nonprotein nitrogen. This research was the outgrowth of the study of the uric acid content of the blood of the new-born carried out by us in association with Kingsbury³ in our laboratories.

The purpose of the investigation was to determine, first, whether the other nitrogenous constituents were high at birth and then gradually decreased to the adult normal figure as is the case with uric acid, and, second, to study the sugar content.

The blood was collected from the superior longitudinal sinus of the new-born in a glass syringe just before the 10 a. m. nursing period. Ten c.c. were expelled into a bottle containing 20 mg. of potassium oxalate dried in a thin film over the bottom and sides. The excellent system of Folin⁴ was used for the analyses. This method is of great benefit in the study of new-born bloods because of the great economy of material.

Table 1 shows the values for the blood sugar, nonprotein nitrogen, urea nitrogen, preformed creatinin and creatin plus creatinin for the following ages: 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 16 and 43 days, respectively. The infants were breast fed; in a few cases it was necessary to complement the mother's milk as stated in the table.

Table 2 shows the intake of milk for each infant before the collection of the blood sample.

1. Howland, J., and Marriot, W. McK.: *Tr. Am. Pediat. Soc.* **28**:202, 1916.

2. Pettibone, C. J. V., and Schlutz, F. W.: *Am. J. Dis. Child* **10**:206, 1915.

3. Sedgwick, J. P., and Kingsbury, E. B.: *Am. J. Dis. Child*, **14**:98, 1917.

TABLE 1.—BLOOD ANALYSES OF INFANTS OF VARIOUS AGES

Case	Sex	Age, Days	Non- protein Nitro- gen	Urea N	Creat- inin	Creatin plus Creat- inin	Sugar, per Cent.	Remarks
Y. 17611	♂	3	59.5	18.9	1.8	10.6	0.07	
H. 18694	♂	3	44.5	17.5	2.0	6.6	0.09	
S. 18753	♀	3	50.0	18.0	1.3	5.3	0.08	
G. 17634	♀	3	61.0	13.0	1.9	9.6	0.07	
W. 17661	♀	4	48.5	15.7	1.7	7.6	—	
H. 18678	♀	4	52.5	22.5	1.9	8.4	0.10	
D. 18729	♀	4	47.0	14.9	1.9	5.7	0.11	
S. 18725	♀	4	39.6	16.2	1.7	5.1	0.07	
J. 17686	♀	5	47.1	10.7	1.9	6.1	0.08	
W. 17630	♀	5	59.5	15.8	2.0	10.6	0.06	
S. 17644	♀	5	43.4	31.6	2.2	8.5	—	Mother syphilitic
A. 17673	♀	5	49.0	15.1	1.7	6.6	0.11	
J. 17647	♀	5	94.2	14.5	1.8	7.1	0.07	Jaundice
B. 17795†	♀	5	2.0	15.0	1.9	6.4	0.08	Jaundice
B. 17796†	♀	5	44.6	13.9	1.9	6.5	0.05	
S. 17787	♀	5	—	13.4	1.8	6.8	0.07	Jaundice
L. 17798	♀	5	44.5	16.1	1.9	6.0	0.07	Jaundice
G. 17812	♀	5	—	13.4	1.8	6.6	0.07	
A. 18634	♀	5	33.5	16.0	1.7	6.4	0.08	
S. 17610	♀	6	48.1	20.2	1.4	9.0	0.09	
W. 17629	♀	6	37.3	10.5	1.4	7.4	0.08	
H. 17805	♀	6	—	23.5	1.6	5.8	0.07	
S. 17968	♀	6	32.8	—	1.5	5.4	—	
S. 17709	♀	6	45.0	18.2	1.6	6.0	0.09	
H. 17708	♀	6	45.0	12.4	1.5	5.7	0.08	
A. 18429	♀	6	30.1	9.4	1.5	6.4	—	
C. 18429	♀	6	35.0	15.2	2.6	5.2	0.07	
S. 17830	♀	7	26.5	14.5	1.7	6.8	0.07	
T. 17995	♀	7	42.4	—	1.8	5.1	0.09	
S. 18329	♀	7	47.0	14.3	1.9	5.9	—	
R. 18358	♀	7	38.2	12.9	1.6	5.8	0.08	
H. 18345	♀	7	48.0	15.0	1.7	7.5	0.08	Unexplained tem- perature
S. 17806	♀	8	36.7	12.2	1.6	7.2	0.10	
McC. 17837	♀	8	32.2	12.3	1.5	7.0	0.08	
B. 18237	♀	8	50.0	13.3	1.8	6.0	0.11	
C. 18305	♀	8	35.5	8.3	2.0	5.5	0.07	
H. 18421	♀	8	33.2	9.8	2.2	5.0	0.10	
J. 17720	♀	9	39.1	12.4	1.9	8.4	0.07	
G. 18269	♀	9	42.2	17.0	1.7	6.0	0.10	
McG. 18273	♀	9	36.7	9.8	1.8	5.8	0.11	
F. 18710	♀	9	37.5	12.5	1.2	9.1	0.10	
T. 17532	♀	10	32.9	11.7	1.5	11.8	0.08	
S. 18217	♀	10	33.3	14.0	1.7	6.2	0.09	
P. 18127	♀	10	25.2	10.6	1.5	6.1	0.06	
G. 18311	♀	11	34.0	8.0	1.6	5.3	0.08	
F. 18036	♀	12	32.8	11.5	1.6	6.1	0.08	
A. 18109	♀	12	22.5	9.8	1.7	5.2	0.06	
S. 18625†	♀	12	24.5	8.4	1.6	4.9	0.10	
P. 18383	♂	13	37.7	10.4	2.1	5.0	0.09	
H. 17309†	♂	43	23.6	13.6	1.4	9.4	0.99	
H. 17920	♂	16	43.1	—	2.0	5.2	0.67	

* Twins.

† Premature.

♀ Female.

♂ Male.

TABLE 2.—DIET OF INFANTS

Case	Birth Weight, Gm.	Days																Average per day for seven days preceding, 480.
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
		B. M.-Comp.	B. M.-Comp.	B. M.-Comp.	B. M.-Comp.	B. M.-Comp.	B. M.-Comp.	B. M.-Comp.	B. M.-Comp.	B. M.-Comp.	B. M.-Comp.	B. M.-Comp.	B. M.-Comp.	B. M.-Comp.	B. M.-Comp.	B. M.-Comp.	B. M.-Comp.	
H. 1	18664	0	15	160														
H. 2	18753	90	20 40	80														
H. 3	17634	0	0	20	80													
H. 4	17634	0	5	105	225													
H. 5	18678	0	0	170	280													
H. 6	18729	15	85	185	0	0												
H. 7	17634	0	20	0	20	215												
H. 8	17634	0	20	145	300	295												
H. 9	17634	0	35	10	250	295												
H. 10	17634	0	30	70	125	195												
H. 11	17634	0	10	15	55	100												
H. 12	17634	0	0	50	70	150												
H. 13	17634	0	0	60	300	190												
H. 14	17634	0	0	0	0	0												
H. 15	17634	0	0	0	0	0												
H. 16	17634	0	0	0	0	0												
H. 17	17634	0	0	0	0	0												
H. 18	17634	0	0	0	0	0												
H. 19	17634	0	0	0	0	0												
H. 20	17634	0	0	0	0	0												
H. 21	17634	0	0	0	0	0												
H. 22	17634	0	0	0	0	0												
H. 23	17634	0	0	0	0	0												
H. 24	17634	0	0	0	0	0												
H. 25	17634	0	0	0	0	0												
H. 26	17634	0	0	0	0	0												
H. 27	17634	0	0	0	0	0												
H. 28	17634	0	0	0	0	0												
H. 29	17634	0	0	0	0	0												
H. 30	17634	0	0	0	0	0												
H. 31	17634	0	0	0	0	0												
H. 32	17634	0	0	0	0	0												
H. 33	17634	0	0	0	0	0												
H. 34	17634	0	0	0	0	0												
H. 35	17634	0	0	0	0	0												
H. 36	17634	0	0	0	0	0												
H. 37	17634	0	0	0	0	0												
H. 38	17634	0	0	0	0	0												
H. 39	17634	0	0	0	0	0												
H. 40	17634	0	0	0	0	0												
H. 41	17634	0	0	0	0	0												
H. 42	17634	0	0	0	0	0												
H. 43	17634	0	0	0	0	0												
H. 44	17634	0	0	0	0	0												
H. 45	17634	0	0	0	0	0												
H. 46	17634	0	0	0	0	0												
H. 47	17634	0	0	0	0	0												
H. 48	17634	0	0	0	0	0												
H. 49	17634	0	0	0	0	0												
H. 50	17634	0	0	0	0	0												
H. 51	17634	0	0	0	0	0												
H. 52	17634	0	0	0	0	0												
H. 53	17634	0	0	0	0	0												
H. 54	17634	0	0	0	0	0												
H. 55	17634	0	0	0	0	0												
H. 56	17634	0	0	0	0	0												
H. 57	17634	0	0	0	0	0												
H. 58	17634	0	0	0	0	0												
H. 59	17634	0	0	0	0	0												
H. 60	17634	0	0	0	0	0												
H. 61	17634	0	0	0	0	0												
H. 62	17634	0	0	0	0	0												
H. 63	17634	0	0	0	0	0												
H. 64	17634	0	0	0	0	0												
H. 65	17634	0	0	0	0	0												
H. 66	17634	0	0	0	0	0												
H. 67	17634	0	0	0	0	0												
H. 68	17634	0	0	0	0	0												
H. 69	17634	0	0	0	0	0												
H. 70	17634	0	0	0	0	0												
H. 71	17634	0	0	0	0	0												
H. 72	17634	0	0	0	0	0												
H. 73	17634	0	0	0	0	0												
H. 74	17634	0	0	0	0	0												
H. 75	17634	0	0	0	0	0												
H. 76	17634	0	0	0	0	0												
H. 77	17634	0	0	0	0	0												
H. 78	17634	0	0	0	0	0												
H. 79	17634	0	0	0	0	0												
H. 80	17634	0	0	0	0	0												
H. 81	17634	0	0	0	0	0												
H. 82	17634	0	0	0	0	0												
H. 83	17634	0	0	0	0	0												
H. 84	17634	0	0	0	0	0												
H. 85	17634	0	0	0	0	0												
H. 86	17634	0	0	0	0	0												
H. 87	17634	0	0	0	0	0												
H. 88	17634	0	0	0	0	0												
H. 89	17634	0	0	0	0	0												
H. 90	17634	0	0	0	0	0												
H. 91	17634	0	0	0	0	0												
H. 92	17634	0	0	0	0	0												
H. 93	17634	0	0	0	0	0												
H. 94	17634	0	0	0	0	0												
H. 95	17634	0	0	0	0	0												
H. 96	17634	0	0	0	0	0												
H. 97	17634	0	0	0	0	0												
H. 98	17634	0	0	0	0	0												
H. 99	17634	0	0	0	0	0												
H. 100	17634	0	0	0	0	0												
H. 101	17634	0	0	0	0	0												
H. 102	17634	0	0	0	0	0												
H. 103	17634	0	0	0	0	0												
H. 104	17634	0	0	0	0	0												
H. 105	17634	0	0	0	0	0												
H. 106	17634	0	0	0	0	0												
H. 107	17634	0	0	0	0	0												
H. 108	17634	0	0	0	0	0												
H. 109	17634	0	0	0	0	0												
H. 110	17634	0	0	0	0	0												
H. 111	17634	0	0	0	0	0												
H. 112	17634	0	0	0	0	0												
H. 113	17634	0	0	0	0	0												
H. 114	17634	0	0	0	0	0												
H. 115	17634	0	0	0	0	0												
H. 116	17634	0	0	0	0	0												
H. 117	17634	0	0	0	0	0												
H. 118	17634	0	0	0	0	0												
H. 119	17634	0	0	0	0	0												
H. 120	17634	0	0	0	0	0												
H. 121	17634	0	0	0	0	0												
H. 122	17634	0	0	0	0	0												
H. 123	17634	0	0	0	0	0												
H. 124	17634	0	0	0	0	0												

Table 3 shows the average values for the blood constituents each day from the third to the twelfth day of life.

TABLE 3.—AVERAGE VALUES FOR BLOOD ANALYSES

Age, Days	Nonprotein Nitrogen	Urea Nitrogen	Creatinin	Creatin plus Creatinin	Sugar, per Cent.	Number of Analyses on Which Average Was Made
3	52.7	16.8	1.7	8.0	0.07	4
4	46.9	17.3	1.8	6.7	0.09	4
5	45.2	15.9	1.8	7.5	0.07	11
6	38.4	15.6	1.5	6.3	0.08	8
7	40.4	14.1	1.7	6.2	0.08	5
8	37.5	10.5	1.8	6.1	0.09	5
9	28.8	12.9	1.6	7.3	0.09	4
10	30.4	12.1	1.5	8.0	0.07	3
11	34.0	8.0	1.6	5.3	0.08	1
12	26.6	9.9	1.6	5.4	0.08	3
13	37.7	10.4	2.1	5.0	0.09	1
16	43.1	—	2.0	5.2	0.07	1
43	23.6	13.6	1.4	9.4	0.09	1

In the adult the normal values for nonprotein nitrogen are 25 to 35 mg. per hundred c.c. of blood, urea nitrogen, 12 to 15 mg. per hundred c.c.; creatinin, 1 to 3 mg. per hundred c.c.; creatinin plus creatin, 6 mg. per hundred c.c., and sugar from 0.08 to 0.12 per cent.

A comparison of the values for normal new-borns with those of adults shows that the nonprotein nitrogen is high during the first few days of life and then decreases gradually; this is also true of creatin plus creatinin. The urea nitrogen is near the upper limit of the adult normal, creatinin is within the normal limits, and the percentage of sugar is near the lower limit, but this may be accounted for by the fact that Folin states that lower values are obtained by his method than the older methods for sugar.

SUMMARY

Analyses of the blood of normal new-borns show that the values for creatin plus creatinin and nonprotein nitrogen are high during the first few days of life corresponding with the high values for uric acid during that period, established in this laboratory before.³ The creatinin and sugar values are essentially the same as the adult normal values, and the urea nitrogen is near the maximum normal value for adults.

A similar study on older infants and children by Schlutz of this department will appear shortly.

We wish to thank Dr. W. R. Shannon, teaching fellow in the Pediatric Department of the Graduate School, for obtaining the blood specimens for us.

ALLERGY IN INFANTS AND CHILDREN *

OSCAR M. SCHLOSS, M.D.

NEW YORK

During the past seven years, I have had opportunity to study 122 cases of allergy in children. Observations derived from the study of these cases and animal experiments pertaining to the subject seem of sufficient importance to report. Despite the relative newness of the subject, the literature has become large, especially concerning bronchial asthma. It is foreign to the object of this paper to review the literature. I propose to consider only such aspects of allergy with which my own work has been concerned.

The following topics will be discussed:

- I. The Cutaneous Test.
- II. Temporary Desensitization. Antianaphylaxis.
- III. The Nature and Origin of the Idiosyncrasy.
 - (a) Nature of sensitization.
 - (b) Origin of sensitization.
- IV. Clinical Types of Allergy.
 - (a) The hyperacute type. Urticaria, angioneurotic edema, asthma and symptoms of shock.
 - (b) Bronchial asthma.
 - (c) Urticaria.
 - (d) Angioneurotic edema.
 - (e) Erythema multiforme.
 - (f) Eczema.
 - (g) Acute dermatitis.
 - (h) Gastro-enteric disturbances in infants.
 - (i) Cyclic disturbances in children.

V. Treatment.

I. THE CUTANEOUS TEST

During the past few years I have used the cutaneous test entirely as opposed to the intracutaneous test. This was done only after having made a series of tests by both methods on normal patients and on patients suffering from definite food idiosyncrasy. Such tests were made on 100 infants and children not apparently suffering from disturbances due to food, and on thirty who suffered from definite symptoms due to the ingestion of some variety of food. In most instances, solutions of the proteins used for the intradermal test were passed through a Berkefeld filter and preserved with tricresol. In case much of the protein was removed by the filter, filtration was omitted. The activity of each preparation was determined by tests on cases of food

* From the Department of Pediatrics, Cornell University Medical College

idiosyncrasy. It is unnecessary to give the statistics in detail, but the results seemed definitely to warrant the following conclusions:

The intracutaneous test is more sensitive. In three patients, later proved to have a mild idiosyncrasy to milk, intracutaneous tests were positive while cutaneous tests were negative. This seems the only point in favor of the intracutaneous test.

Against it is the fact that it is apt to be misleading. Pseudo-reactions occur which are difficult to interpret, and in some instances patients give reactions which seem positive despite the lack of clinical evidence that the substance tested causes any symptoms. Many vegetable proteins are difficult to obtain in a form soluble in physiologic sodium chlorid solution, but are soluble only in alkaline solvents. Such solutions cannot be used for intradermal tests. To insure sterility, the proteins used must be prepared carefully, which adds considerable technical difficulty. On two occasions I have seen severe infections due to such tests. Another objection is that a very sensitive patient may be made seriously ill by the injection of even a minute amount of the protein to which he reacts. In consideration of these objections it seems that, for general use, the cutaneous test is the one to be chosen.

The materials used for the test are of great importance. Certain foods rich in protein, such as milk or egg, may be used unaltered. With foods poor in protein, it is best to use the proteins in a comparatively pure form. Such proteins are now on the market.

It is best to use a preparation representing all of the proteins of the food since sensitiveness to the individual proteins varies in different individuals. For example, in six cases of egg idiosyncrasy, ovomucoid seemed to be the most active protein. In three other cases, however, pure ovomucoid did not cause a cutaneous reaction while marked reactions were caused by ovalbumen.

In milk lactalbumen has been, in my experience, the most active protein. In only two of fourteen cases of milk idiosyncrasy investigated did casein cause a skin reaction, and then to a much less marked degree than lactalbumen.

Of the vegetable proteins, the proteoses are apt to cause the most marked cutaneous reactions. This is probably the result of greater solubility and diffusibility.

A problem of fundamental importance is, what constitutes a reaction? A positive reaction consists of a distinct urticarial wheal surrounded by a zone of erythema in the presence of a negative control test. If the reaction is at all marked, the wheal is 5 mm. or more in diameter. The wheal indicating a true reaction is always irregular in outline; the edges are never sharply circumscribed. The irregularity is caused by edema spreading along the lymph spaces, and is quite characteristic. This appearance has been likened to the pseudopodia

of an aneiba. All doubtful or suspicious reactions should be considered negative. In such cases, the test should be repeated at some other time, but, until a reaction is obtained which is distinct in the presence of a negative control test, it is best to disregard it.

A control test is always necessary. If the forearm is selected for the site of the inoculation it is important that the control be placed nearest the bend of the elbow. The skin is more sensitive at this place, and for this reason, a traumatic reaction is more likely to occur. In this event, if an inoculation be made at this point and the control be made in a less sensitive part, a reaction that is purely traumatic may be called positive. It is also quite true, that the degree of reaction in sensitive persons varies, dependent on the site of inoculation. For example, in a patient sensitive to egg, a cutaneous test made near the bend of the elbow is apt to cause a much greater reaction than one made near the wrist. This has been demonstrated in a number of cases.

This brings up the question of the influence of the irritability of the skin on the reaction. There are certain persons, especially some affected with factitious urticaria, in whom a simple scratch will cause a distinct urticarial wheal. In such a person, the control and all inoculations will cause the development of reactions which appear positive. In some instances, this condition may be especially confusing as the wheals caused by the inoculation of proteins may be larger than the wheal caused by the control. Even though this may seem to indicate a true reaction, I am strongly of the opinion that such tests should be disregarded unless the difference between control and inoculations is very marked and is evident on repeated tests.

Marked irritability of the skin is often present in patients affected with urticaria and asthma rendering the performance of satisfactory tests impossible. The condition, however, is often transitory, and a time may be found when satisfactory tests can be made.

There seems little doubt that a true reaction is due to protein alone. Careful experiments made some years ago¹ demonstrated that the cutaneous reaction was elicited by the protein constituents of foods, and that extracts free from protein were inert. Such experiments have been repeated on three additional patients, one sensitive to pork, one sensitive to egg, almonds and wheat, and the third sensitive to milk. In no instance was it possible to cause a reaction by any material free from protein. It is unnecessary to give the experiments in detail, as this has been done in a previous communication.

1. Schloss, O. M.: A Case of Allergy to Common Foods, *Am. J. Dis. Child.* 3:341, 1912.

Sufficient evidence has accumulated to make it reasonably certain that a positive skin reaction in the presence of negative control tests is indicative that the patient is sensitive to the protein to which he reacts. In most instances it can be demonstrated that the protein causing a reaction is capable of producing symptoms. Exceptions to this are very rare, but I have seen six cases in which it was impossible to prove that the substances to which the patient reacted were responsible for symptoms. Two of the patients were affected with asthma, two with urticaria and two had recurring attacks of abdominal pain and vomiting. All of these patients reacted to more than four different food proteins, but eliminating from the diet the foods to which they reacted had no effect on the symptoms.

It is difficult to offer a satisfactory explanation for these unusual occurrences. It seems possible that the patients were sensitive to more foods than was indicated by the skin tests, and for this reason all foods capable of causing a reaction were not eliminated. At the time the tests were made, the patients may have been temporarily desensitized to other foods capable of causing symptoms so that even though these foods caused no cutaneous reaction at that time, sensitiveness may have returned later to a sufficient degree to be responsible for symptoms. The possibility of such an occurrence is indicated by evidence to be given later.

The greatest limitations of the cutaneous test lie in another direction. A negative cutaneous test is not conclusive. This is especially true in individuals with gastro-enteric symptoms. I have observed five cases of undoubted idiosyncrasy to cow's milk with persistently negative cutaneous tests. These infants regularly developed diarrhea, abdominal pain and vomiting when the smallest amounts of raw whole milk, fat-free milk, whey or lactalbumin were ingested. Moderate amounts of thoroughly boiled milk or milk protein were tolerated. The skin test was positive in two other patients with identical symptoms. I believe that this discrepancy may be dependent on the lack of skin sensitization in some cases and its presence in others.

Another influence limiting the utility of the skin test is the occurrence of temporary desensitization.

II. TEMPORARY DESENSITIZATION. ANTI-ANAPHYLAXIS

It is well known that after recovery from anaphylactic shock, a guinea-pig is temporarily desensitized. For a certain period injections of the protein to which it was sensitive are without effect. After a variable time sensitiveness returns. I have been able to demonstrate the same occurrence in infants.²

2. Schloss, O. M.: Allergy in Infants and Children, *Tr. Am. Pediat. Soc.*, 1914.

Observations were conducted on four infants, three of whom were sensitive to egg and one to milk. Cutaneous tests were positive, and the ingestion of egg or milk caused marked urticaria. Following the occurrence of symptoms, the cutaneous reaction disappeared and the foods could be ingested with no ill effect. After a period varying from twenty-seven to forty-five days, cutaneous sensitiveness returned and symptoms were caused by ingestion of the toxic foods.

TABLE 1.—POSITIVE CUTANEOUS REACTION TO EGG *

Date	Cutaneous Reaction	Symptoms	Date	Cutaneous Reaction	Symptoms
1/ 5	++	Urticaria	3/18	—	
1/ 6	—		3/10	—	
1/ 7	—	None	3/12	—	
1/ 8	—		3/14	—	None
1/10	—		3/16	—	
1/12	—	None	3/18	—	
1/14	—		3/20	—	
1/16	—	None	3/22	—	None
1/18	—		3/24	+	
1/20	—	None	3/26	--	Moderate urticaria
1/22	—		3/28	—	
1/24	—	None	3/30	—	
1/26	—		4/ 1	—	
1/28	—	None	4/ 3	—	
1/30	—		4/ 5	—	
2/ 1	—		4/ 7	—	None
2/ 3	—		4/ 9	—	
2/ 5	—	None	4/11	—	
2/ 7	—		4/13	—	
2/ 9	--+	Severe urticaria	4/15	—	
2/10	—	None	4/17	—	
2/12	—		4/19	—	
2/14	—		4/21	—	None
2/16	—	None	4/23	—	
2/18	—		4/25	—	
2/20	—		4/27	—	
2/22	—	None	4/29	—	
2/24	—		5/ 1	—	None
2/26	—		5/ 3	—	
2/28	—	None	5/ 5	—	
3/ 2	—		5/ 7	—	
3/ 4	—		5/ 9	—	
3/ 6	—	None	5/11	--	Severe urticaria

* Baby G. A., aged 5 months. Eczema. Seen first on Jan. 5, 1915. Ingestion of one quarter of an egg white caused severe general urticaria fifteen minutes after ingestion on four occasions. The egg white was given on the days on which notations are made under "symptoms."

The practical significance of this occurrence is obvious. In a sensitive individual, cutaneous tests may be negative because of temporary desensitization despite the fact that the patient suffers at times from definite symptoms due to allergy. Whether there is a stage of desensitization in all cases of allergy after the development of symptoms is doubtful. For this to occur, it is probably necessary for the patient to ingest a comparatively large amount of the offending protein. This was demonstrated in one case. The patient reacted to the ingestion of egg by a mild urticaria. The ingestion of about one-twentieth of an egg white was followed by the appearance of a few urticarial wheals. Every alternate day for six days the same amount of egg white was

given, and in each instance slight urticaria developed. The cutaneous reaction to egg remained positive. The patient was then given about one-third of an egg white. Severe urticaria developed, the cutaneous reaction disappeared for forty-six days, and during this period one-third of an egg white could be ingested without discomfort. The cutaneous reaction then reappeared and the ingestion of egg white caused urticaria.

The patients used for these investigations developed urticaria as the only symptom of protein sensitization. Whether patients with other symptoms, such as bronchial asthma, also become desensitized after an attack is unproved, but by analogy seems probable.

III. THE NATURE AND ORIGIN OF THE IDIOSYNCRASY

(a) *The Nature of Sensitization.*—There seems to be but little question that allergy in the human is closely analogous to anaphylaxis in the experimental animals. This has been proved in some cases of food idiosyncrasy. The only conclusive proof is the transfer of sensitization to animals. This is difficult and fails in most cases, but it has been accomplished. Bruck³ obtained positive results in a case of idiosyncrasy to shell fish.

In a case of egg idiosyncrasy previously reported by me,⁴ it was possible passively to sensitize guinea-pigs by injections of the patient's blood serum. I have repeated this experiment in seventeen other cases with three positive results. Nine of the seventeen patients were of the clinical type which most closely simulates anaphylaxis in the guinea-pig. These patients were extremely sensitive to milk, beef or egg, cutaneous reactions being caused by very dilute solutions of the constituent proteins. The ingestion of the smallest amounts of these foods caused the immediate development of marked swelling of the lips and tongue with local urticarial lesions. Severe asthma developed almost immediately, and within a short time marked general urticaria. These patients showed signs of prostration and in several instances became alarmingly ill.

In three cases of this type, positive results were obtained. These observations are of sufficient importance to cite one in some detail.

CASE.—B. F., aged 6, developed severe symptoms from the ingestion of egg, beef, walnuts and almonds. As far as could be ascertained, symptoms occurred the first time these foods were ingested. An older brother had suffered from idiosyncrasy to egg from which he recovered.

The patient had eczema from the age of 15 months and still had periodic eruptions. Asthma began when he was 2 years old, and had been practically continuous since. Marked cutaneous reactions were caused by the proteins to

3. Bruck: Experimentale Beiträge zur Aetiologie und Pathogenese der Urticaria, Arch. f. Dermatol. u. Syphilis **96**:241, 1909.

4. Loc. cit.

which he was sensitive. Three c.c. of the patient's blood (citrated) were injected intraperitoneally into each of four guinea-pigs. Twenty-four hours later three of the animals (weight 260 gm., 286 gm. and 320 gm., respectively) were given intraperitoneal injections of 1.5 c.c. of egg white diluted with an equal amount of physiologic sodium chlorid solution.

All three animals became severely ill with the usual symptoms of anaphylactic shock, and died at the end of two and one-half, three and six hours, respectively. The lungs showed the usual distention and petechial hemorrhages were present in the pleura, pericardium and myocardium. The fourth animal (weight 306 gm.) was given an intraperitoneal injection of egg white which had been freed of protein by treatment with heat and acetic acid, and alcohol. Three c.c. of the protein free extract were given by intraperitoneal injection. Slight signs of irritation were present for a few minutes but no further symptoms developed. Three controls were given intraperitoneal injections of 3 c.c. of citrated blood from a normal person. Twenty-four hours later they were given 1.5 c.c. of the same egg white solution used in the experiments. No symptoms developed.

The results in the other two cases were practically identical. One of the patients was sensitive to milk, the other sensitive to egg.

In six other instances the blood of patients suffering from identical symptoms did not passively sensitize guinea-pigs. In two patients, the idiosyncrasy was quite as marked as in the ones from whom positive results were obtained. The other four patients showed the same type of disturbance, but to a lesser degree.

Four of the remaining eight patients used for similar observations suffered from severe asthma due apparently to foods. Four patients suffered from eczema and gave positive skin reactions to cow's milk. It was attempted passively to sensitize guinea-pigs with the blood of these patients, but without success.

(b) *Origin of Sensitization.*—A question of considerable interest is, how is the sensitization acquired? In a great number of cases, there is a family history of disturbances probably due to allergy. This occurrence has been considered by Cooke and Van der Veer,⁵ Longcope⁶ and others.

In eighty cases I was able to obtain a satisfactory history on this point. In forty cases there was a definite history of allergy in the parents, brothers or sisters. In seven cases the history was positive, but applied to the grandparents. In the remaining thirty-three cases no history of similar disturbances in the family was obtainable. Of these thirty-three persons, however, sixteen developed symptoms the first time some food was eaten so that the condition was in all probability congenital, although there was no history indicating that it was inherited. In the remaining seventeen cases the food in question was eaten some time before the characteristic symptoms appeared. The only explanation for this group is that sensitization was acquired.

5. Cooke, R., and Van der Veer, A. Human Sensitization, *J. Immunol.* **1**: 201, 1916.

6. Longcope, W. T.: The Susceptibility of Man to Foreign Proteins. *Am. J. M. Sc.* **152**:625, 1916.

In reference to origin of sensitization the cases may be divided into two groups:

1. Congenital.

(a) Inherited. A definite history of similar disturbances in the parents or grandparents. Symptoms developing the first time a given food is eaten.

(b) History of inheritance lacking. No family history of sensitization, but a toxic action of some food the first time it is ingested.

2. Acquired.

One of the greatest differences between cases of sensitization in the human and experimental animals is the fact that so many of the cases in the human are congenital or inherited. Despite this dissimilarity, there is a definite group of cases in which sensitization is unquestionably acquired and the symptoms in these patients are essentially the same as in the inherited cases. In some cases the history indicates definitely the time at which sensitization occurred. This was true of five cases which I have had the opportunity to observe. Two infants were given egg white during attacks of diarrhea. The egg white was taken several days and did not cause the least disturbance. When egg was fed several months later, serious symptoms occurred. One breast fed infant was given whey for several days during an attack of diarrhea. No symptoms occurred. Several months later, when milk was fed, the infant was extremely sensitive. Another breast fed infant was given a milk formula for a few days under similar circumstances. He also became sensitive and developed severe disturbances when weaning was attempted.

It has been shown by a number of investigators, Rosenau and Anderson,⁷ Wells⁸ and others, that guinea-pigs may become sensitized when fed foreign proteins. Two factors may play a part in sensitization of infants through the gastro-enteric tract. First, an inflamed or irritated enteric mucous membrane. It has been shown by Lust,⁹ Worthen and myself,¹⁰ and others, that foreign protein is absorbed by many infants under such conditions. Another factor may be the feeding of a foreign protein for a short time only. Bearing on this, this is experimental evidence which is worth consideration.

7. Rosenau and Anderson: Bull. No. 29, Hygienic Laboratory, April, 1906.

8. Wells: The Biological Reactions of the Vegetable Proteins, J. Infect. Dis. **8**:66, 1911.

9. Lust: Die Durchlässigkeit der Magendarmkanales für Heterologes Eiweiss bei Ernährungestarten Säuglingen, Jahrb. f. Kinderh. **67**:244, 283, 1913.

10. Schloss and Worthen: The Permeability of the Gastro-Enteric Tract of Infants to Undigested Protein, Am. J. Dis. Child. **11**:342, 1916.

Wells¹¹ found that guinea-pigs fed on zein (a protein from corn) for some time could not be sensitized by injections of this protein. He then conducted experiments which indicated the possibility that guinea-pigs fed on corn became immune so that it was impossible to sensitize them by intraperitoneal injections of zein. It seemed of sufficient importance to ascertain whether this phenomenon occurred regularly and whether sensitization always preceded the immunity.

For this purpose I have conducted feeding experiments with egg and milk.¹² Two groups of 16 young guinea-pigs were given each day about 5 gm. of dried egg white or dried milk in addition to their usual food. A group of control animals were given their usual diet only. Counts of the eosinophil blood cells were made each day. Every three days one animal from each group was given an intraperitoneal injection of egg and milk, respectively, to ascertain if sensitization had occurred. It was found that between the seventh and the sixteenth day there was an increase of the eosinophil cells, and at approximately the same time the animals developed distinct symptoms after intraperitoneal injections of egg or milk, showing that they had become sensitized. At the time one animal was found to be sensitized, the experiment was repeated on a second in confirmation. After sensitization had occurred, two of the remaining animals were tested at 15-day intervals. It is unnecessary to give the experimental details, but at the end of two months none of the animals developed anaphylactic symptoms when given intraperitoneal injections of egg or milk protein. The salient features of these experiments are shown in Table 2 and protocols 3, 4 and 5.

PROTOCOL 3.—Showing occurrence of sensitization to egg protein after feeding egg white for ten days.—Guinea-pigs 81 and 82. Fed on regular diet of oats, hay and fresh vegetables for seven days. Daily blood counts showed no eosinophilia. Guinea-pig 81 had a maximum count of 2.2 per cent. and Guinea-pig 82 of 1.8 per cent. during this period. After this period of preliminary observation, from 7 to 8 gm. of egg white were given each day. Eosinophilia was evident on the eighth day in No. 81, and on the ninth day in No. 82. On the tenth day of egg feeding both animals were given 1.5 c.c. of egg white by intraperitoneal injection. Both became ill. Immediate roughening of coat, itching of nose, dyspnea and weakness. Temperature of No. 81 fell 6 degrees, and of No. 82 8 degrees. Both animals were ill for from three to four hours, and gradually recovered. Three days later both animals were given intraperitoneal injections of 1.5 c.c. of egg white. No symptoms occurred, showing the presence of anti-anaphylaxis.

PROTOCOL 4.—Demonstrating that sensitization to egg protein is present after continuous feeding of egg white for thirty-two days.—Guinea-pigs 88 and 92 were fed the usual diet. From 7 to 8 gm. of powdered egg white were added to the diet on the seventh day. The usual eosinophilia developed. After the twenty-sixth day the eosinophil cells were practically normal. On the thirty-

11. Loc. cit.

12. These experiments were reported before the American Society for Clinical Investigation in 1915.

second day of egg feeding both animals were given 1.5 c.c. of egg white by intraperitoneal injection. Both developed the usual symptoms of anaphylactic shock. No. 88 died fifty-two minutes after the injection. The lungs showed the characteristic distention. Petechial hemorrhages were in the pericardium and peritoneum. No. 92 was quite ill, but began to improve after one and one-half hours and recovered. Four days later it was given 1.5 c.c. of egg white by intraperitoneal injection. No symptoms occurred showing the presence of anti-anaphylaxis.

TABLE 2.—SHOWING EFFECT OF FEEDING EGG WHITE ON THE EOSINOPHIL BLOOD CELLS OF A GUINEA-PIG *

Date, 1912	Diet	Eosinophil Cells, per Cent.	Date, 1912	Diet	Eosinophil Cells, per Cent.
7/ 6	Regular	1.0	7/26	About 7 gm. of powdered egg white added	11.6
7/ 7	Regular	1.2			
7/ 8	Regular	0.5	7/27	About 7 gm. of powdered egg white added	6.7
7/ 9	Regular	0.8			
7/10	Regular	0.5	7/28	About 7 gm. of powdered egg white added	10.6
7/11	Regular	1.3			
7/12	Regular	1.1	7/29	Regular, egg omitted	7.2
7/13	About 7 gm. of powdered egg white added	0.5	7/30	Regular, egg omitted	2.1
			7/31	Regular, egg omitted	1.3
7/14	About 7 gm. of powdered egg white added	0.8	8/ 1	Regular, egg omitted	2.1
			8/ 2	Regular, egg omitted	0.5
7/15	About 7 gm. of powdered egg white added	0.8	8/ 3	Regular, egg omitted	1.2
			8/ 4	Regular, egg omitted	1.4
7/16	About 7 gm. of powdered egg white added	1.2	8/ 5	Regular, egg omitted	1.2
			8/ 6	Egg white added	2.1
7/17	About 7 gm. of powdered egg white added	2.1	8/ 7	Egg white added	6.7
			8/ 8	Egg white added	7.3
7/18	About 7 gm. of powdered egg white added	1.2	8/ 9	Egg white added	10.6
			8/10	Egg white added	7.3
7/19	About 7 gm. of powdered egg white added	2.3	8/11	Egg white added	6.4
			8/12	Egg white added	6.6
7/20	About 7 gm. of powdered egg white added	3.1	8/13	Egg white added	4.3
			8/14	Egg white added	4.0
7/21	About 7 gm. of powdered egg white added	4.3	8/15	Egg white added	3.2
			8/16	Egg white added	1.2
7/22	About 7 gm. of powdered egg white added	8.9	8/17	Egg white added	3.1
			8/18	Egg white added	1.2
7/23	About 7 gm. of powdered egg white added	14.4	8/19	Egg white added	0.05
			8/20	Egg white added	0.05
7/24	About 7 gm. of powdered egg white added	7.6	8/21	Egg white added	1.0
7/25	About 7 gm. of powdered egg white added	10.9			

PROTOCOL 5.—*Showing the absence of sensitization to egg protein after feeding egg white for sixty-two days. Also, the impossibility of sensitizing such animals by intraperitoneal injections of egg protein.*—The conditions of this experiment were essentially the same as those outlined in protocols 3 and 4. On the sixty-second day of feeding powdered egg white, Guinea-pigs 93 and 94 were given intraperitoneal injections of 1.5 c.c. of egg white. Both animals seemed somewhat uncomfortable for a few minutes, but developed no noteworthy symptoms.

To determine whether these animals were sensitized by this injection of egg protein, they were given a second injection of 1.5 c.c. of egg white fifteen days after the first. No noteworthy symptoms developed. This experiment was repeated on two other animals with identical results.

The results in the group of animals fed milk were practically identical with those cited, and, therefore, require no special comment. These experiments show that the ingestion of foreign protein by guinea-

* Guinea-pig 83. Regular diet of oats, hay and carrots, lettuce or cabbage.

pigs causes the development of immunologic reactions. The animals became sensitized to the protein fed so that parenteral administration caused the symptoms of anaphylactic shock. When small amounts of protein are fed not enough is absorbed from the enteric tract to cause symptoms, although sufficient apparently passes into the circulation to produce sensitization.

In connection with these experiments it seemed of importance to ascertain whether sufficient protein could be ingested to cause symptoms in sensitized animals. Five guinea-pigs, about 300 gm. in weight, were sensitized to egg white and five to cow's milk. The animals were starved for fourteen hours and then were given oats and carrots which had been thoroughly saturated with concentrated solutions of dried milk and egg white, respectively. Four of the animals of the group which had been sensitized to egg, and three in the group sensitized to milk developed severe diarrhea and were quite ill for twenty-four hours. Increase in the number of eosinophil cells in the blood was noted in all. One animal in the group tested with milk and two in the group treated with egg developed no definite symptoms, except that they did not run around the cage and were very quiet. Of interest is the fact that all three of the animals developed eosinophilia, 9.3, 10.8 and 13.4, respectively. It seems unnecessary to give all the experiments in detail, but one protocol will be given. The others were identical.

Guinea-pig 133, given sensitizing dose of 0.05 c.c. of egg white by intraperitoneal injection Aug. 10, 1911. Daily counts of the eosinophil cells were as follows: August 8, 1.3 per cent.; August 9, 2.1 per cent.; August 10, 1 per cent.; August 11, 1.9 per cent.; August 12, 1.6 per cent.; August 13, 2 per cent.; August 14, 1.6 per cent.; August 15, 0.0 per cent.; August 16, 2.3 per cent.; August 17, 17.1 per cent.; August 18, 2.4 per cent.; August 19, 2.6 per cent.; August 20, 0.05 per cent.; August 21, 1.3 per cent.

Thirteen days later, after starvation for twelve hours, the animal was given oats saturated with egg white of which it ate greedily. Within five minutes the coat became rough, the animal huddled up in the corner of the cage and the breathing became increased and somewhat labored. Almost immediately it began to have watery stools. Counts of the eosinophil cells were as follows.

	Eosinophil Cells, Per Cent
Five minutes after ingestion of egg white.....	0.05
Twenty-five minutes after ingestion of egg white.....	7.3
Forty minutes after ingestion of egg white.....	14.2
One and one-half hours after ingestion of egg white.....	6.3
Three hours after ingestion of egg white.....	2.1
Five hours after ingestion of egg white.....	1.2
Seven hours after ingestion of egg white.....	11.3

The rectal temperature fell from 100.7 F. just before ingestion of the egg to the lowest level of 94.6 F. one hour later. The animal was quite ill for twelve hours and then slowly improved and seemed practically well twenty-four hours later.

Each of the animals was given an intraperitoneal injection of 1 c.c. of egg white three days later, and none of them developed anaphylactic shock. Evidently, the ingestion of the protein to which they had been sensitized was sufficient to cause desensitization. This would seem to prove that the symptoms were due to anaphylaxis.

Two series of control were carried out. Three animals which had not been sensitized, after twelve hours starvation, were fed egg at the same time that the experimental animals were fed. None of the control animals developed symptoms. Four other control animals were sensitized to egg white at the time the experimental animals were. They received an intraperitoneal injection of egg white at the same time as the experimental animals. All died with characteristic symptoms of anaphylactic shock.

These experiments demonstrate that in sensitized guinea-pigs feeding large amounts of the protein to which they are sensitive may cause distinct symptoms. These symptoms are mainly intestinal and are not typical of anaphylactic shock. That these symptoms were of such origin, however, is indicated by the fact that the animals became desensitized and a later injection of the protein caused no symptoms.

If the results of these experiments could be proved to apply to human beings it would be of fundamental importance, offering an explanation not only for many cases of food idiosyncrasy, but, perhaps, also for certain nutritional disturbances. This proof, however, is lacking. That such reactions may occur in infants is suggested by the observations of Berger.¹³ He found that infants previously fed exclusively on the breast, almost regularly developed eosinophilia from seven to ten days following the administration of cow's milk.

IV. CLINICAL TYPES OF ALLERGY

(a) *The Hyperacute Type with Urticaria, Asthma and Symptoms of Shock.*—This type of allergy is most commonly due to milk or egg, occasionally to beef. It may be caused by other foods, but much less frequently than by those mentioned. This type of disturbance is observed also in susceptible individuals after the injection of horse serum.

In such cases very little of the food is actually ingested, as the infant spits it out of his mouth or vomits immediately after it has been swallowed. Within a few minutes there is a swelling of the lips, tongue and buccal mucous membrane. Symptoms of collapse occur, and the patient becomes drowsy or somnolent. Shortly afterward there is marked general urticaria. Asthma commonly occurs immediately after the food is swallowed and is usually severe. It occurs in many cases, but not in all. It may be absent in the earlier attacks, but present in later ones. Sneezing and conjunctival congestion are usually pro-

13. Berger, H. C.: Eosinophilia Occurring in Infants Following the Ingestion of a Foreign Protein, *Arch. Pediat.* **33**:743, 1916.

nounced. All of the symptoms usually appear within a few minutes, and the severe symptoms usually subside within an hour or two. The urticaria may last from sixteen to twenty-four hours.

The diagnosis in this type of food idiosyncrasy is usually made by the parents or by the patient. The occurrence of the symptoms is directly traced to the ingestion of a particular food.

(b) *Bronchial Asthma*.—That bronchial asthma is often due to allergy is now a matter of common knowledge. The very careful and painstaking work of Walker has shown that the allergy may be due to the proteins of food, pollens, epidermis of animals and bacteria.

It is unnecessary for me to consider the subject of asthma in detail as my clinical experience has been relatively small in comparison with that of Walker. Such experience, however, is entirely in accord with his.

(c) *Urticaria*.—The fact that urticaria is commonly due to sensitization has led to the attempt to attribute all urticaria to this cause. In actual experience, however, this relationship is impossible to prove. In addition to the patients in whom urticaria follows regularly the ingestion of some food, I have made cutaneous tests on sixty patients. Ten persons had to be excluded owing to the factitious urticaria. In only ten cases were the tests positive. Six of these patients reacted to many proteins, 9, 8, 7, 6, 5 and 4, respectively. These proteins were constituents of foods almost essential to a normal diet. Owing to this cause, or lack of cooperation, it was impossible to prove a causal relationship by elimination of the foods in question. In four cases, however, the reaction was positive to only three or fewer proteins, and it was possible to demonstrate the exact relationship by feeding experiments or immunization.

I did not test cases of urticaria with the proteins from bacteria or pollens, and it is quite possible that had this been done, more positive results would have been obtained. Also, the tests were not done at different times so that it is possible that some of the patients were desensitized at the time the tests were made.

(d) *Angioneurotic Edema*.—My experience with cases of angioneurotic edema is similar to that with urticaria. Several of the patients who regularly developed urticaria after eating certain foods were also affected with angioneurotic edema, often coincident with the urticaria. In most instances the relationship of the cutaneous symptoms to the particular food were known. Exclusive of these, fourteen patients with angioneurotic edema were tested. Three had factitious urticaria and cutaneous tests were unreliable. Two of the remaining eleven reacted to skin tests, one to milk and wheat and the other to egg and beef. The causal relationship was demonstrated in both by dietetic

experiment. Both patients suffered from recurring attacks of local edema of the skin. Such attacks occurred every few weeks, and lasted a day or two.

(e) *Erythema Multiforme*.—The relationship between urticaria, angioneurotic edema and erythema multiforme is well known. Osler¹⁴ particularly has grouped them together. I have made cutaneous tests on seven patients suffering from erythema multiforme and in one patient a relationship to food was demonstrated, both by cutaneous tests and by eliminating from the diet the food to which the patient reacted. This patient was sensitive to pork and was immunized by injections of pig's blood serum.

(f) *Eczema*.—The relationship of eczema to food idiosyncrasy is of peculiar interest and has been touched on in a previous communication.¹⁵ A large number of patients with food idiosyncrasy either suffer from eczema or suffered from it in infancy. A vast proportion of infants or young children with bronchial asthma had eczema during infancy, and in many there was a distinct family history of eczema. For purposes of description, I shall place my cases into two groups: 1. Those patients under 16 months of age. 2. Those over 16 months of age.

In the first group there were fifty-three cases. Forty gave cutaneous reactions. Thirteen reacted to not more than three foods, and twenty-seven reacted to more than three foods. Thirty-four reacted to egg white despite the fact that egg had never been eaten. To ascertain whether the cutaneous reaction was actually indicative of idiosyncrasy, eleven patients were fed small amounts of egg. All developed definite symptoms. It is quite obvious, however, that the idiosyncrasy to egg had nothing to do with the causation of eczema in these patients. Thirty-six of the patients reacted to cow's milk, and as this was the basis of their food, it was considered that the milk was, perhaps, responsible for the eczema. In artificially fed infants this is difficult to prove, as it is almost impossible to keep up their nutrition on foods free from milk protein. That the milk protein may be the cause of the eczema was demonstrated in six patients. These patients, all of whom had eczema, were given a mixture consisting of protein free milk (lactose and mineral salts),¹⁶ washed butter and soy bean protein. The amounts of fat, sugar and protein were approximately the same as they had been receiving. In all cases the eczema improved

14. Osler: On the Visceral Manifestations of the Erythema Group of Skin Diseases, *Am. J. M. Sc.* **127**:1 (Jan.) 1904.

15. Schloss, O. M.: Allergy in Infants and Children, *Tr. Am. Pediat. Soc.*, 1914.

16. Made according to Osborn and Mendel.

markedly in twenty-four hours and practically disappeared in three days. This mixture, however, caused diarrhea and vomiting in four of the patients and for this reason further observations were not made. The experience of Blackfan¹⁷ with infantile eczema is practically identical. He found that severe eczema would often disappear after elimination of milk from the diet. It is obvious, however, that definite proof of the allergic nature of infantile eczema must depend on the development of a food, free from milk protein, which is capable of sustaining nutrition.

Indirect evidence, however, is furnished by the common experience that infants with eczema will often do best on milk in which the protein is partially denaturized. Such preparations are soured milk and milk which has been subjected to heat or to peptonization.

The opinion is current among pediatricians that sugar and fat are the usual offending constituents of milk in causing eczema. This is in accord with clinical experience. That these substances are the direct cause of all cases, however, has not been clearly demonstrated.

In the second group — individuals over 16 months of age — there were twenty-four cases. Ten gave positive cutaneous tests. The eczema in the positive cases presented certain rather definite characteristics. The skin was dry, scaly and much indurated. The areas affected were uniform in appearance. Weeping areas were present only during periods of marked exacerbation. The skin of the hands and forearms, the bends of the elbows and over the popliteal space were the usual sites of the disease. The skin of the face and forehead was often dry and scaly, but not usually indurated. During periods of exacerbation, the face, chest and back were affected at times.

Six of the patients reacted to so many different proteins that a confirmatory therapeutic test was impossible. In the remaining four patients, after eliminating the offending articles of diet, the eczema either disappeared or was greatly improved. One case will be cited.

C. N., aged 5 years, suffered from eczema since 6 months of age. Various forms of medication and various restrictions of diet had been tried without avail. At the time he came under observation, he had been on a diet consisting only of a very small amount of skimmed milk, egg and farmaceous vegetables for more than a year. His weight was 31 pounds. The red blood cells numbered 3,500,000, and the hemoglobin 10 gm. per hundred c.c. (Palmer). (Normal from 11 to 14 gm. per hundred c.c.)

A cutaneous test was positive to egg. All other tests were negative. He was given a diet containing all varieties of food except egg. The eczema disappeared within a week and during the course of two years, there has been no recurrence. He has gained 14 pounds in weight and the blood count is normal.

17. Blackfan, K. D.: Cutaneous Reactions from Proteins in Eczema, *Am. J. Dis. Child.* **11**:441, 1916.

It seems impossible to express any definite opinion at present concerning the allergic nature of infantile eczema. Many infants with eczema give cutaneous reactions, in most instances to egg or milk protein. It is impossible at present to feed an infant satisfactorily on a diet free from milk protein so that a definite relationship is difficult to prove. The evidence available is suggestive that some cases at least, are due to food idiosyncrasy.

(g) *Acute Dermatitis*.—I have observed three cases of acute dermatitis (acute eczema) due to pollens.¹⁸ The type of disturbance was similar in all. The onset usually was sudden. The skin of the arms, abdomen and inner surface of the thighs became red and indurated with intense itching. At the onset there were usually a few circular areas affected. These spread, coalesced at the edges within a day or so, giving rise to a uniform involvement of the skin. Viewed with the naked eye, there were no papules, but with a lens, minute papules could be seen. The rash was influenced to a degree by local treatment, but continued for several weeks or months. In all essentials this rash corresponds to acute eczema.

In both cases the rash was due apparently to pollens. In both, ragweed and dandelion were the causative agent.

The patients had been affected each season for three years. Immunizing injections of the extracts of the pollens were given to two patients, and during that season there was no occurrence of the rash. Immunization was repeated the following year. One patient developed a slight rash on one thigh which lasted for a few days and then disappeared entirely. The other patient was free from the eruption.

A third patient has been observed who was subject to the same type of skin lesion. The dermatitis occurred about the middle of August for the past three years and lasted until the middle of September or the first of October. Cutaneous tests showed a marked reaction to ragweed and a slight reaction to goldenrod. Immunizing injections of ragweed pollen were given during May and June, 1919. These apparently had no marked benefit, for the rash appeared as before, but about ten days later. A frost occurred early in September, killing all ragweed in the vicinity. The rash disappeared at this time and did not recur.

(h) *Gastro-Enteric Disturbances. Vomiting, Diarrhea*.—That certain infants develop acute gastro-enteric disturbances when fed small amounts of raw cow's milk, is a matter of common observation. In some cases, urticaria, angioneurotic edema and marked general disturbances are present in addition to the gastro-enteric symptoms. Patients belonging in this group always give a positive cutaneous reac-

18. Sutton, R. L.: Ragweed Dermatitis, J. A. M. A. **72**:126 (May 3) 1919.

tion to cow's milk protein and symptoms occur immediately after the injection of very small amounts of milk. There seems no doubt of the allergic nature of the disturbances in cases of this type.

In a second group of cases, the symptoms are less acute and may not occur until the milk has been taken for several days. The symptoms consist of loss of appetite followed by vomiting and diarrhea, irritability and, at times, fever. One often encounters patients in whom such disturbances follow regularly the ingestion of small amounts of milk, and such symptoms occur until the patient's tolerance to cow's milk has been increased. These patients, rarely, show a positive cutaneous reaction to cow's milk protein, and it is difficult to determine definitely whether the symptoms are really due to sensitization to the proteins of cow's milk or merely to disordered digestion or to abnormal bacterial action in the intestinal tract.

The methods available for investigation of this problem do not permit of a definite solution, but that the condition may be caused by protein sensitization is indicated by a number of observations.

1. *In some cases the symptoms do not occur when thoroughly boiled milk is fed.* The following case is cited in illustration.

Baby E. H., aged 3 months, was seen first Jan. 11, 1919. The weight was 8 pounds 6 ounces, only 8 ounces more than the birth weight. The baby had been breast fed for one week and since that time was fed on various types of infant foods. The ingestion of raw cow's milk in various modifications was always followed within a few days by loss of appetite, vomiting, diarrhea and prostration. Cow's milk, which had been brought to a boil was better tolerated but led to the same type of disturbance, though to a much less degree.

On a diet of dried milk, the infant gained weight and acted normally. February 1, one teaspoonful of whey from cow's milk was added to each feeding. Three days later the usual symptoms occurred, which disappeared after elimination of the whey. February 10, one-half teaspoonful of raw whole milk was added to each feeding with identical results. February 23, one teaspoonful of whey which had been kept at boiling temperature for one hour was added to each feeding. No symptoms occurred. The same amount of pasteurized whey was added March 6. The usual symptoms developed.

After recovery from this attack, one drop of raw milk was given in each feeding. The amount was increased one drop each day for one week, and then five drops each day. Within two months, it was possible to feed a formula containing raw milk on which the infant thrived normally.

This patient was able to take a formula made up of dried cow's milk without symptoms, but regularly became ill after the addition of small amounts of raw or pasteurized cow's milk or whey. The chemical nature of the food elements in dried milk and raw milk are identical, and it seems hardly possible that the symptoms were due to the additional food elements contained in such small amounts of whey or milk. It also seems difficult to believe that bacteria contained in the milk or whey caused the symptoms, especially as pasteurized whey caused the same reaction as raw whey.

It seems evident that the symptoms were due to something present in the milk which was rendered inert by heat. It was also possible to establish tolerance by feeding increasing amounts of raw milk. From the evidence at our disposal it seems probable that the symptoms were due to a specific reaction to raw cow's milk.

Additional cases serve as further evidence.

Baby T. C., aged 5 months, was admitted to the New York Nursery and Child's Hospital June 3, 1910. The patient had done very poorly on various modifications of cow's milk. On a formula made of evaporated milk the infant began to thrive, and for three weeks had gained in weight and was free from digestive disturbances. The weight on admission was 9 pounds 8 ounces. Three weeks later it was 11 pounds.

Careful analysis of the evaporated milk formula was made on three occasions. The average was as follows: Fat, 2.05 per cent.; sugar, 6.21 per cent.; protein, 2.35 per cent. Formulas of analyzed raw cow's milk of a composition as nearly identical as possible were then given. The formulas were pasteurized in a Freeman pasteurizer. Within three days the infant began to refuse part of its food, vomited and had loose stools. After a period of starvation, it was again put on the evaporated milk formula and within a few days began to gain weight.

Similar experiments were made on eight other infants with identical results in four. In two cases, the infants appeared to do quite as well on the pasteurized milk formulas as on the one made from evaporated milk. Two infants did not gain as rapidly, but did not develop pronounced digestive symptoms.

These observations show that disturbances occurred in five infants fed on raw cow's milk which were absent when evaporated milk of the same composition was fed. These disturbances could not have been caused by the chemical ingredient of the foods. They were obviously caused by something in milk which was changed either by evaporation or by age. That these disturbances may have been caused by bacteria in the raw milk cannot be disproved entirely. This possibility, however, is minimized by the fact that the milk was the purest obtainable, and that the formulas were all pasteurized. It certainly seems more probable that the difference was due to the effect of heat on the proteins.

2. *Infants suffering from identical symptoms may show a positive cutaneous reaction to cow's milk.* In two infants with histories identical with those cited, there was a positive cutaneous reaction to cow's milk. One case will be cited in illustration.

A. B., aged 4½ months, was seen first May 3, 1919. He had been artificially fed since birth, but had done poorly on various modifications of cow's milk and proprietary foods up to the age of 3 months. On each food he had suffered from periodic attacks of vomiting and diarrhea with resulting loss of weight.

At this time he weighed 8 pounds 3 ounces. The attending physician prescribed a proprietary food which consists of thoroughly heated cow's milk, starch and sugar. The infant did well on this diet, gained regularly and was free from digestive disturbances. On several occasions the physician added

small amounts of raw milk (from $\frac{1}{2}$ to 1 teaspoonful) to each feeding. Gastro-enteric symptoms occurred on each occasion. They appeared from twenty-four to forty-eight hours after the first feeding of raw milk. On one occasion, there was an urticarial eruption twenty-four hours after the feeding was commenced.

Cutaneous tests to cow's milk protein were positive. The reactions were slight but distinct. Casein caused no reaction, but lactalbumen caused a distinct one. The infant was immunized by adding whey to the formula. At first only one drop was added to each feeding, the amounts being increased slowly at first and then more rapidly. Immunization was started May 7. May 28, the cutaneous reaction was much less marked. It had disappeared entirely June 16, at which time the infant was receiving $1\frac{1}{2}$ ounces of whey in each feeding in addition to the proprietary food. The feedings were then changed to a modification of cow's milk which were well taken and caused no symptoms.

The type of case under discussion presents symptoms commonly seen in infants who are difficult to feed. The only essential difference is the fact that in the type of case I have cited these disturbances followed regularly the ingestion of very small amounts of cow's milk.

It is far from my intention to advance the hypothesis that the digestive disturbances of infants fed on cow's milk are usually due to protein sensitization. Such disturbances are at present attributed to bacterial action in the intestinal tract, to feeding too large amounts of fat, sugar or protein, or to a special intolerance of the infant to some milk constituent. A discussion of the validity of these various views is beyond the scope of this paper. My only reason for considering this type of case is to present evidence which indicates that in some cases idiosyncrasy to the protein of cow's milk is a factor to be considered.

(i) *Cyclic Disturbances in Children.*—The clinical history of certain types of digestive disturbances in children strongly suggests an allergic origin. Such disturbances are characterized by recurrent attacks of vomiting, diarrhea and fever. These disturbances occur at intervals of from two weeks to three months.¹⁹ I have made cutaneous tests in twenty cases of this type, and in only two were the results positive. Both patients presented histories which were practically identical. One will be cited.

J. R., aged 8 years, had suffered from recurring attacks of fever, slight abdominal pain and nausea for four years. The attacks came at intervals varying from two weeks to two months, and lasted from three to five days. The mother had observed that when egg or egg-containing foods were omitted the attacks did not occur. Four months before coming under observation, the attacks had increased in frequency and occurred every thirteen to seventeen days. Egg in all forms was eliminated from the diet, and for three months no attacks had occurred.

The patient had eczema as an infant and had several attacks of severe urticaria. A positive cutaneous reaction was given by egg protein. All other tests were negative. The patient was immunized by feeding increasing amounts of dried egg white. During immunization one of the regular attacks occurred.

¹⁹ Such disturbances are frequently due to focal infections, often of the tonsils.

The onset was sudden, with fever (103 F.), slight abdominal pain and nausea. The symptoms lasted three days and then disappeared. Immunization was completed nine months ago and the patient has remained free from attacks.

The second patient suffered from similar attacks and was also sensitive to egg protein. On a diet free from egg, he had no attacks.

V. TREATMENT

(a) *Treatment by Eliminating the Foods to Which the Patient Reacts.*—The treatment of cases of food idiosyncrasy by eliminating the offending foods is simple provided the patient is not sensitive to a great number. In some instances the number of foods to which the patient reacts is so large that this form of treatment is impossible.

It is important that the food is eliminated not only in a pure state, but also as an ingredient of other foods. This is particularly true of milk and egg which are so largely used in various dishes.

Many patients with food idiosyncrasy recover spontaneously. This is true particularly of the congenital type due usually to milk or egg. The symptoms in this group are usually so pronounced and follow so regularly the ingestion of the particular food that the patients are practically always aware of the idiosyncrasy. Usually the disturbance becomes less and less, and ultimately the patient is able to eat the food in question without discomfort. This, however, does not occur in all cases.

(b) *Treatment by Desensitization.*—Desensitization may be accomplished by hypodermic injection of the protein to which the patient is sensitive. This form of treatment is particularly applicable to disturbance caused by pollens.

To desensitize to foods by this means would seem the most rational procedure, but there is one considerable difficulty—to obtain sterile proteins in a soluble and a non-irritating form for this purpose. With a number of the foods this is impossible. Many of the food proteins after separation are soluble only in alkaline solvents which would be very irritating if injected into the tissues.

I have attempted to desensitize five patients with idiosyncrasy to egg by this method. All of these patients gave a marked reaction to ovomucoid which is readily soluble in normal saline and is only slightly irritating. It is, therefore, well adapted for use in injections. All patients with idiosyncrasy to egg do not react to ovomucoid, and therefore treatment by injections of this substance is not always applicable.

Of the five patients treated, two disappeared from observation before the treatment was complete. Neither had shown any improvement while under observation. The remaining patients became completely immune. The initial injection was 0.0001 mg. of ovomucoid. Injections were given at intervals of five days, and the dose was

doubled at each injection. The progress of immunity was gaged by the cutaneous reaction. The process of immunization required two months, three months and three and one-half months, respectively. The final dose of ovomucoid was 0.1 gm., 0.18 gm., and 0.21 gm., respectively.

Reaction from the injections occurred several times in two of the patients. In one case they were local and consisted entirely of the development of a large urticarial wheal and erythema. The second patient on two occasions developed moderate general symptoms, asthma and vomiting, in addition to a local reaction.

Immunization by hypodermic injections was tried in three cases of idiosyncrasy to cow's milk. The casein was removed from fat free milk by rennin. The whey was dialysed to remove sugar and salts and then pasteurized. The protein content was based on a total nitrogen estimation and the preparation preserved with tricresol. The method of procedure and dosage were practically identical to those used in immunizing to ovomucoid. One patient was lost track of after the fourth injection. The other two became desensitized.

(c) *Immunization by Feeding*.—This method of treatment consists of the administration of gradually increasing amounts of the offending protein or food until toleration is established. By this means it is possible to immunize a considerable proportion of cases of idiosyncrasy to egg or milk.

The procedure is relatively simple. If the patient is old enough, dry egg or milk protein or dried egg white or milk is given in capsules three times a day. Needless to say, the initial dose should be very small; if the patient is very sensitive, from 2 to 5 mg. in each capsule is sufficient. While the dose is small, it is necessary to use milk sugar or starch as a diluent. The rate of increase varies somewhat, dependent on the sensitiveness of the patient. Reactions should be avoided, if possible. As a rule, it is sufficient to begin with three capsules a day, and to give an additional capsule each succeeding day. Within a week, capsules containing a larger amount of the food or protein should be used, because otherwise the patient would be ingesting too many capsules and too much diluent in proportion to the actual amount of protein. Ultimately the pure protein or food is given.

The amount of the dried food or protein required for desensitization varies considerably, but is always large. Usually at the end of the treatment, the patient receives from 15 to 30 gm. of the dried protein or food in twenty-four hours. While smaller doses are apparently sufficient to desensitize to a considerable degree, yet the completion of the process requires the ingestion of a very large amount.

Children under 3 years of age are usually unable to swallow capsules, and for them this method of administering the protein or food is not possible. As a substitute, a solution can be used, but owing to the direct contact with the buccal and pharyngeal mucosa the initial dose must be very small. For example, an infant, 1 year of age, sensitive to milk, developed marked swelling of the tongue and lips after taking 1 drop of milk diluted with 1 teaspoonful of water. A reaction was also caused by $\frac{1}{5}$ drop of milk. In this case the initial dose was $\frac{1}{20}$ of a drop of milk, three times a day. When this method is used the increase in dosage must be very gradual at first.

During the process of immunization cutaneous tests should be made to determine the progress. It is best at the onset to determine approximately the highest dilution to which a positive reaction is given. Done in this way, the cutaneous test offers a more accurate index to the progress of desensitization than if a strong solution were used each time. Desensitization by this method requires from three to six months. This form of treatment has been used in twenty-four cases of idiosyncrasy to milk. All of the patients were markedly sensitive, and at the conclusion of the treatment were able to ingest the food without discomfort.

After desensitization is accomplished, it is necessary for the patient to take regularly a moderate amount of the food to which he was sensitive. Otherwise, he will again become sensitive and symptoms may occur. In this event, however, the symptoms are less severe than before treatment. Desensitization can be brought about very quickly by resuming treatment.

It occasionally happens that patients who have been desensitized have a return of symptoms despite the continuous ingestion of a small amount of the food. It is probable in such cases that the amount ingested was too small. Under these conditions, usually the symptoms consist only of urticaria, or, perhaps, slight swelling of the lips and tongue. It is only necessary to give treatment for a few days with large amounts of the food to cause a return of desensitization.

I have been able to follow twelve of the patients who were desensitized from three to seven years. All of these patients are now quite immune and can eat, without discomfort, the foods to which they were sensitive.

FORDYCE'S DISEASE AS PSEUDOKOPLIK SPOTS AND A CAUSE OF MISTAKES IN THE DIAGNOSIS OF MEASLES *

JOSEPH C. REGAN, M.D.

BROOKLYN

Fordyce's disease is a chronic disease of the mucous membrane of the mouth and lips which is characterized by the presence "of whitish or yellowish, scanty or abundant, discrete, aggravated and often coalescent miliumlike bodies, occurring more especially on the inside of the mouth, laterally along the line of the teeth as far back as the last molar, and possibly somewhat less frequently on the vermillion or mucus and inner surface of the lips."¹ The lesions are from pinpoint to pinhead in size, and usually of a pale buff or oatmeal color. They are almost invariably imperceptible to touch, being situated on a level with the buccal mucosa, but at times they may send out hairylike projections which penetrate the mucous membrane. As a rule, the patient is unconscious of the condition, as subjective symptoms are lacking. The disease is most commonly encountered between the ages of 20 and 40, but it has also been observed in young children. Fordyce,² to whom is due the honor of the first description of the condition, considered it to be the result of a granular change in the protoplasm of the cells of the affected mucosa. Some other investigators, however, as a result of histologic study contend that the lesions are to be attributed to slightly, moderately, or sometimes markedly developed sebaceous glands. Heuss³ believes that the disease is favored by catarrhal conditions of the mucous membrane, while White,⁴ in a series of sixty-five cases, found that 70 per cent. of his patients suffered from various skin diseases intimately associated with disorders of the sebaceous glands.

The condition has proven especially interesting to me from a contagious standpoint inasmuch as these lesions are not infrequently mistaken for Koplik's spots, even by physicians who are familiar with the appearance of the latter. On several different occasions, patients, usually older children or adults, were sent into the hospital with an incorrect diagnosis of measles, the examination on entrance showing

* From the Kingston Avenue Hospital of the Bureau of Hospitals, Department of Health of New York City, Dr. R. J. Wilson, Director.

1. Stelwagon, H. W.: *Treatise on Diseases of the Skin*, Philadelphia, 1907, pp. 1122, 1123.

2. Fordyce, J. A.: *J. Cutan. Dis.*, 413, 1896.

3. Heuss: Quoted by Stelwagon, loc. cit.

4. White, C. J.: *J. Cutan. Dis.*, 23:97, 1905.

all the typical symptoms of German measles, the buccal mucosa failing to show Koplik's spots, but presenting a typical picture of Fordyce's disease.

That mistakes in diagnosis between measles and German measles should originate at times in this way is not surprising, because the similarity between the symptoms of the two diseases is at times quite pronounced, and this analogy is rendered closer still because of the deeper hue of color, reddish pink to deep red, which the buccal mucous membrane often assumes in the latter disease. This congestion is frequently slightly more pronounced at the site of Fordyce's spots giving them the appearance of an acute lesion. It is, moreover, possible that this latter disease is temporarily aggravated by the local congestion of the surrounding mucosa and that this accounts in part for the greater prominence of these lesions during the acute infection.

Recently a child was admitted into the hospital with the symptoms of mild scarlatina. A diagnosis of measles had been made by the family physician evidently based, in part, on the presence in the mouth of those pseudo-Koplik spots.

We have quite frequently seen Fordyce's spots mistaken for Koplik's spots in patients ill with various contagious diseases whose buccal mucosa was being examined daily for the appearance of the true spots, owing to the exposure of the patients to a previous case of measles. Likewise, children sent into the hospital with a diagnosis of laryngeal diphtheria or influenzal croup have at times been isolated as possible beginning cases of measles with a catarrhal laryngitis, the subsequent examination showing the suspicious lesions to be nothing more than a few Fordyce spots.

The possibility of these pseudo-Koplik's spots leading to errors in diagnosis when they are present in patients who develop maculopapular rashes from serum, antitoxin, etc., accompanied by fever, is also a point which should be kept in mind. We have seen a diagnosis of probable measles in part based on their presence in a suspected case of antitoxin rash. Not infrequently Fordyce's disease exists in patients who develop Koplik's spots. In such instances the two types of lesions when seen together are so distinct as to permit readily of their differentiation.

Well marked and pronounced examples of Fordyce's disease are unusual, although not exceptional in young children. Slightly marked cases, however, are frequently seen, even in infancy, but the lesions are, as a rule, few in number. They are small, discrete, and situated well back on the buccal mucosa, often just posterior to the site of the last molar teeth, and are visible only on careful inspection of the mucous membrane. This characteristic grouping of the spots on the buccal mucosa assists greatly in their identification.



I



II



III



IV

I. Koplik's spots, early stage—Leukemic eruption, eruptive, minute, red, subcuticular spots with red areola.

II. Koplik's spots, more advanced stage—Leukemic eruption, eruptive, minute, red to whitish yellow or blue spots, situated on oral mucosa (anterior buccal mucosa).

III. Fordyce's disease in children—Nagell's disease (not strictly red blood mucosa), with the catmeal colored spots crowded in patches on buccal mucosa.

IV. Fordyce's disease in older patients—showing slight areolar enlargement. Often have around them in patients with German measles.

The two types of lesions are, as a rule, so dissimilar that a differential diagnosis usually offers no difficulties. Koplik's spots evolve in from three to six days, passing through various stages, and then disappear, while in Fordyce's disease the spots persist after the symptoms of the acute malady have subsided. Color of the lesions, their distribution, size and location differ. At an early stage Koplik's spots are minute, white or semivesicular spots, with a surrounding red areola, situated immediately on the surface of the buccal mucous membrane, and inside of the lips, having no particular arrangement as to the upper and lower rows of teeth. Later on, as they become more numerous, the adjacent areolae fuse to form a diffuse red background on which the numerous milky white spots stand out elevated, and at times are somewhat coalescent. At a still later period of development, the buccal mucosa begins to return to its normal coloration, and the lesions are seen as small milkish white specks on the membrane resembling nothing more than some minute particles of food, especially milk, which have adhered temporarily to the mucous membrane. Finally, just before they disappear, that may change to almost transparent and merely visible vesicles.

Fordyce's spots, on the contrary, have the characteristics mentioned above. They are yellowish white or of a café-au-lait color, larger than Koplik's spots, often coalescent, situated right in the superficial layers of the mucous membrane and without a definite areola.

A point to be kept in mind in examining for Koplik's spots, one which often accounts for errors in diagnosis, especially when the lesions are poorly defined, is that one should use daylight and preferably sunlight in looking for them. Artificial light is decidedly unsatisfactory.

CONCLUSION

1. Among the conditions of the mouth which may simulate Koplik's spots, Fordyce's disease deserves a place greater in importance than that accorded aphthous stomatitis.

2. Fordyce's spots are especially apt to be mistaken for Koplik's spots when they exist in patients who develop German measles. The similarity between the clinical symptoms of the two diseases is further increased by the presence of these pseudo-Koplik spots. The resemblance between the two types of lesions in such cases may be rendered closer still, because of the changes which the buccal mucosa undergoes in German measles which gives it a deeper coloration than normal. Being often more prominent at the site of Fordyce's spots, it gives them the appearance of an acute lesion.

3. Fordyce's disease is quite frequently mistaken for early Koplik spots in patients ill with various contagious diseases and exposed to

measles, whose buccal mucosa is being examined daily for the appearance of the true spots.

4. Children sent into a contagious hospital as cases of laryngeal diphtheria or influenzal croup may, at times, be isolated as possible beginning cases of measles owing to the presence of these lesions. (Catarrhal laryngitis plus coryza, being one of the modes of onset of measles, a careful examination of the buccal mucosa is made on the admission of all croup cases.)

5. The possibility of these pseudo-Koplik spots leading to errors in diagnosis when they are present in patients with suspicious looking maculopapular eruptions from serum or antitoxin, should be borne in mind.

6. Well marked and pronounced examples of Fordyce's disease are unusual in young children. Slightly marked cases are, however, frequently seen even in infancy, but the lesions are so few in number, so small, and often situated so far back on the buccal mucous membrane, and of so nearly the normal color of the mucosa of a child, as usually to be overlooked, except where a careful search is being made for Koplik's spots.

The two types of lesions, Fordyce's spots and Koplik's spots, are, as a rule, so dissimilar that a differential diagnosis offers no difficulties to one familiar with their characteristics. Those unfamiliar with their appearances may, however, readily confuse them. As stated above, the color, arrangement, distribution, evolution, size and location of the two lesions differ in so definite a way as to permit readily of their differentiation.

8. Relative to the examination for Koplik's spots, one fact should be emphasized — to use daylight or sunlight whenever possible.

The writer wishes to thank Dr. R. J. Wilson for affording him the opportunity to carry out this study.

THE BACILLUS OF PFEIFFER IN INFLAMMATIONS OF THE RESPIRATORY TRACT IN CHILDREN *

MARTHA WOLLSTEIN, M.D., AND RALPH C. SPENCE, M.D.

NEW YORK

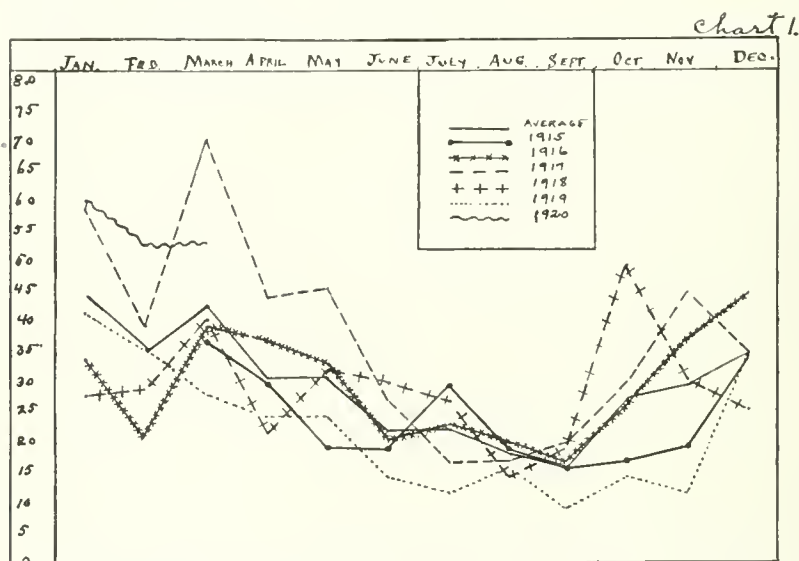
At the Babies' Hospital there are patients with respiratory diseases in the wards at all seasons. The number commences to increase during the latter part of September and during October, rises steadily during November and December, reaches the highest point in January, remains high through February and March, then gradually declines during April and May to reach the lowest point in June, and stays low until the middle of September. The combined curve for the last five years, illustrating the incidence of the respiratory diseases at the hospital, is graphically shown in the accompanying chart. Parallel curves for each of the last five years are also shown. It can be seen that the highest point reached at any time from March 1, 1915, to March 1, 1920, was in 1917, when seventy cases of respiratory disease were admitted to the wards during March. Since the statistics for the city as a whole show but a very slight increase in respiratory diseases in 1917, we can only explain our figures by the increased number of admissions to the hospital. One hundred and fifty babies were admitted during March, 1917, while the average number of admissions during the other four years for the same month was 104. The highest number of respiratory cases admitted during March in any one of the four years was forty-three; the lowest, twenty-eight. The next highest number appeared during January, 1920, which was the beginning of the latest influenza outbreak in New York City.

It is interesting to compare the curve during the epidemic, beginning in October, 1918, with that of the recurrence in 1920. In the former case the incidence of respiratory diseases rose abruptly from the middle of September to the middle of October, then gradually fell below the average at the end of November and remained decidedly below the number reached in any of the other four years until January, 1919, when it rose slightly, but declined in February, and remained below the average throughout the rest of the year. Indeed, during 1919 the admissions for diseases of the respiratory tract at the Babies' Hospital were lower than they had been at any time during the previous four years. The average number for the five years was reached only in the last week of December, when the recurrent epidemic evidently started.

* From the laboratory of the Babies' Hospital.

Since it has been the custom for some years at the Babies' Hospital to examine the sputum of the patients with respiratory diseases for the presence of the bacillus of Pfeiffer, an intensive study to determine the presence of this organism in respiratory and nonrespiratory diseases during an epidemic period was undertaken. The further purpose of our study was to determine the possible influence of the presence of the Pfeiffer bacillus in the sputum on the clinical course and outcome of the cases examined, and also to compare the results with those we had previously obtained in nonepidemic years.

From Jan. 1 to March 20, 1920, or throughout the duration of the latest epidemic of influenza in New York City, 1,000 sputum cultures were studied from children admitted to the hospital wards, from ambulatory cases coming to the dispensary, from the mothers of some of the outdoor patients, from the nurses in the hospital and from the attending and resident staff of physicians.



Combined curve showing incidence of respiratory disease at the Babies' Hospital during the last five years.

Technic.—Plates of oleate agar¹ and of heated blood agar were used in the study of our cultures, one plate being used for each patient. In every instance an effort was made to procure mucus from the lungs or from the upper respiratory tract. This was obtained from the babies by using a curved sterile cotton swab to touch the posterior pharyngeal wall. The mucus was caught on the swab as it was coughed up during this procedure. In the cases in which we were unable to obtain sputum in this way a postnasal culture was taken by turning the

1. Avery, O. T.: J. A. M. A. **71**:2050 (Dec. 21) 1918.

curved part of the swab upward. A small portion of the thickest mucus in the specimen of sputum so obtained was placed near the edge of a Petri plate and rays drawn from it in all directions over the medium. The plates were incubated for forty-eight hours. The colonies were then examined with a hand lens and with the naked eye. A cover slip was placed over that portion of the plate which showed the largest number of small, moist, dewy colonies, and pressed down firmly enough to allow the colonies to become attached to the glass. In this way whole colonies were fixed and stained by Gram's method. Pure cultures were isolated whenever possible.

The children ranged in age from 7 days to 13 years. The majority were less than 2 years old. Two hundred and ninety-four adults were examined. The accompanying table shows the age incidence of the positive and negative cases.

AGE OF POSITIVE AND NEGATIVE CASES

	B. Pfeiffer in Sputum		B. Pfeiffer Not in Sputum		Total
	Number	Per Cent.	Number	Per Cent.	
Under 3 months old.....	11	30	34	70	45
3 to 6 months old.....	36	41	52	59	88
6 to 12 months old.....	71	51	68	49	139
1 to 2 years old.....	97	58	71	42	168
2 to 3 years old.....	50	56	40	44	90
3 to 4 years old.....	44	60	29	40	73
4 to 5 years old.....	28	70	12	30	40
5 to 13 years old.....	39	65	21	35	60
Over 20 years old.....	95	33	169	67	264
	474	47.4	526	52.6	1,000

It will be seen that the frequency of the presence of the Pfeiffer bacillus increased with the age throughout the first five years of life. It was lowest in infants less than three months old and increased in frequency as the age increased during the first year. It was present still more often throughout the second and third years, while the largest percentage of positive cultures was found among children between the ages of 4 and 5 years. This may be explained by a combination of several factors. The children more than 1 or 2 years old are walking and have greater opportunities for becoming infected. They also give better specimens of sputum than do the young infants who are more guarded from contact with infected persons. The low percentage of 33 found among the adults examined is explained largely by the fact that none of them were acutely ill. They were parents, nurses and physicians who were in contact with the patients.

Among our 1,000 cases there were 101 children with pneumonia; 122 patients with other respiratory inflammations, including rhinitis, laryngitis and bronchitis, severe enough to produce a febrile reaction; 473 simple colds without any elevation of temperature; twenty-three

children in whom the respiratory symptoms were complicated by measles either during the prodromal stage or during convalescence; fifteen children with tuberculosis; and finally control cultures on 266 healthy individuals who had had no recent colds.

1. CASES OF PNEUMONIA.—One hundred and one patients were studied. The oldest was 5 years and the youngest was less than 6 weeks of age. Seventy-four of the children showed the presence of the Pfeiffer bacillus in the sputum cultures; twenty-seven did not. The mortality rate of 42 per cent. for the total number of pneumonia cases studied in this series was much lower than that for the pneumonia patients who were admitted to the hospital during the influenza epidemic of 1918, when it reached 57.7 per cent. Thirty-five of the positive cases terminated fatally, and twenty-seven came to necropsy. There were only two cases of lobar pneumonia in our series. In one of the two, broncho-pneumonia was present in another lobe.

Postmortem Bacteriology.—Cultures from the lungs were taken in twenty-two of the twenty-seven cases which came to necropsy after *B. Pfeiffer* had been grown from the sputum during life. The bacillus was cultivated from the lung exudate in twenty, but only three times in pure culture. Pneumococcus was the accompanying organism eight times, staphylococcus in eleven cases, streptococcus only twice, and the diphtheria bacillus in two cases. Pfeiffer bacillus was not found in any of the pleural exudates. In only two cases were the bacilli not found in the lungs at necropsy when they had previously been grown from the sputum during life. In one of these cases the lungs were removed through the empyema wound, and the plate cultures were overgrown with a contaminating bacillus. The other case could not be studied until four days after death, when the cultures were contaminated. Four children died before a sputum culture could be obtained, but the Pfeiffer bacillus was cultivated from the lungs at necropsy. The omission of a sputum culture during life was due to the moribund condition of the baby on admission, and its death soon afterward. Pfeiffer bacilli were found in the heart's blood in only one of the twenty-seven cases that came to necropsy, and in no instance were they found in the blood during life.

Pathology.—The gross pathologic picture was very similar to that noted during the epidemic of October, 1918.² Subpleural and intra-alveolar hemorrhages were a constant feature and congestion of the lungs was very marked. Generalized mucopurulent bronchitis was the rule. In children who died during the first four or five days of the illness the pneumonic areas were peribronchial in distribution and bright red in color. After a longer duration the consolidated areas had

2. Wollstein, M., and Goldbloom, A.: *Am. J. Dis. Child.* **17**:165 (Feb.) 1919.

coalesced to occupy the greater part of several lobes, and purulent infiltration, gray or yellow in color, was apparent along the interstitial septa, around the bronchi, or both. Small abscesses, especially beneath the pleura, were encountered in nine of these cases. The pleura was inflamed in seventeen instances, the exudate ranging from a thin layer of fibrin to a large amount of fluid pus. Pulmonary abscesses occurred more frequently than in the cases studied during the 1918 epidemic,² while the pleura was involved in slightly fewer instances in the present series.

In the twenty cases which came to necropsy and contained the Pfeiffer bacilli in the lungs, there was a family history of infection seven times, while one case was infected in the hospital six days after admission. The temperature of these fatal pneumonia cases ranged from 97 F. to 106 F., running an irregular course with morning remissions. In eleven of the patients the afternoon temperatures exceeded 104 F. The leukocyte counts varied from 8,000 to 45,000, the average being about 19,000, which is far above the normal number of leukocytes for young children. In no instance was there a leukopenia. The three cases in which the Pfeiffer bacillus was found at necropsy in pure culture were infants aged from 4½ to 6 months. All three showed scattered areas of bronchopneumonia throughout both lungs with typical subpleural and intra-alveolar hemorrhages. The leukocytes numbered 8,000, 14,000 and 18,000, respectively. That is, the leukocytes were not diminished in any of the three cases, but were only slightly increased in two cases. In only one were the polymorphonuclears increased in number.

Most of the cases of pneumonia ran an acute course lasting from four days to two weeks. The symptoms in four cases lasted a longer time. Two babies had empyema and died from one to two months after the onset of the pneumonia. One child with miliary tuberculosis lived seven weeks after the onset, and one, which lived five weeks, had otitis media as the only complication. Another patient had had a previous attack of influenzal pneumonia, with Pfeiffer bacilli present in the sputum, from which he recovered one month before his last illness began. The final attack lasted only two days and a pure culture of Pfeiffer bacilli was obtained from the lungs at necropsy. This child probably had a recurrent attack rather than a reinfection.

Twenty-seven pneumonia patients in this series did not have the bacillus of Pfeiffer in their sputum. Seven of them died, and necropsies were performed on six. The Pfeiffer bacilli were recovered from the lungs of two of these children who had died before a second sputum culture could be made. In one case the plate on which the sputum culture was taken was overgrown with staphylococci; and in the other,

with staphylococci and Klebs-Löffler bacilli. At necropsy cultures from the lungs showed many colonies of the bacillus of Pfeiffer, with staphylococci in both, and Klebs-Löffler bacilli in the one in which these organisms had been so abundant in the sputum during life.

In our present series of seventy-four pneumonia patients showing the Pfeiffer bacillus in the sputum, it was possible to follow the entire illness of sixty-five, of whom 53 per cent. died. On the other hand, the twenty-seven pneumonia patients whose sputum did not show the presence of the Pfeiffer bacillus gave a mortality rate of 33 per cent., twenty-two of the cases having been followed throughout the course of the disease. There was, then, a distinctly higher death rate among the children who had pneumonia with the presence of the Pfeiffer bacillus than among those whose sputum did not contain this bacillus, a fact which we had noted in previous years.

2. MEASLES.—Twenty-three babies under 2 years of age were examined either during the prodromal or the convalescent stage of measles; that is, before they were sent to a hospital for contagious diseases, or after dismissal from such a hospital. All had fever, cough and bronchitis at the time the cultures were taken, and fourteen showed Pfeiffer bacilli in their sputum.

3. TUBERCULOSIS.—There were fifteen cases of tuberculosis among the children studied. All were under the age of 2 years. Five carried Pfeiffer bacilli in their sputum. Two of these five cases came to necropsy and the bacilli were recovered from the lungs of both.

4. CASES OF BRONCHITIS AND RHINITIS WITH FEBRILE REACTION.—There were 122 children in our series, all less than 5 years of age, who were ill with respiratory symptoms, but who did not develop pneumonia. The lesion was limited to the nose, pharynx, larynx and bronchi. The temperature of these children reached 105 F. in some instances, and ran a very irregular course, often reaching normal in the early morning. The prostration was not as severe as the temperature would indicate, and all ended in recovery. One hundred and four, or 85 per cent., showed the Pfeiffer bacillus in the sputum.

In no instance was the bacillus of Pfeiffer present in the sputum in pure culture; the accompanying organisms were pneumococcus, staphylococcus, micrococcus catarrhalis, the Klebs-Löffler bacillus, and rarely streptococcus. The high percentage of these nonpneumonia cases with a distinct general reaction, in which the bacillus of Pfeiffer was found, is significant in comparison with the results obtained in our next group.

5. COLDS WITHOUT TEMPERATURE COMPRISING CASES OF RHINITIS AND PHARYNGITIS, BUT WITHOUT PULMONARY INVOLVEMENT OR GENERAL REACTION.—This group comprises 473 cases, the largest number

of any group in our series. Three hundred and eleven were dispensary patients under 12 years of age, and 162 were adults: 12 physicians, 22 nurses and 128 parents who accompanied the children to the dispensary. One hundred and seventy-two, or 55 per cent., of the children showed the presence of the Pfeiffer bacillus in their sputum, and it was found in 43 per cent. of the parents. In 66 per cent. of the twelve physicians from whom cultures were taken during the course of an acute or chronic catarrh of the upper respiratory tract, was the bacillus of Pfeiffer grown from the sputum. Of the nurses with cold, 59 per cent. carried the organism. Altogether, the positive cases in this group numbered 54 per cent., showing the high preponderance of the Pfeiffer bacillus in cases of ordinary head colds at this time.

6. CONTROLS.—As controls, 266 persons without respiratory symptoms of any kind, and with no history of recent colds, were studied. Twenty-nine had the Pfeiffer bacillus in their sputum, or approximately 10 per cent. Ten of these positive cases were older children who were exposed to younger members of the family, brought to the dispensary for acute colds, and in whose sputum Pfeiffer bacilli were found. Only one of the five physicians in this group carried the bacillus of Pfeiffer. Yet all were working among the children with respiratory diseases and were, therefore, exposed to the infection. Only two of the twenty-four nurses in this group were carriers. Sixteen carriers were the parents of children who were brought to the dispensary because they had acute colds, and from fourteen of the sixteen children the bacillus was cultivated. Twice the parent was positive and the child negative. Only two cases remain as unexplained, healthy, carriers. This emphasizes the exceedingly small number of healthy persons who carry the Pfeiffer bacilli in their respiratory secretions, even during the time of an influenza epidemic, unless there is a history of direct exposure. Other observers have found much higher percentages of so-called healthy carriers both in and between epidemics, but their studies were made in camps, institutions, or large cities, where the chances for infection were very great (Opie et al.,³ Lord et al.,⁴ Winchell and Stillman,⁵ Stillman and Pritchett⁶).

In 219 instances it was possible to take cultures in from two to six members of one family and to obtain the respiratory history of the family throughout this epidemic period. In the majority, however, only the mother and one child were studied in a given family. Forty-

3. Opie, E. L., Freeman, A. W., Blake, F. G., Small, J. C. and Rivers, T. M. *J. A. M.* **72**:108 (Jan. 11) 1919.

4. Lord, F. T., Scott, A. C. and Nye, R. N.: *J. A. M. A.* **72**:188 (Jan. 18) 1919.

5. Winchell, A., and Stillman, F. G.: *J. Exper. Med.* **30**:47, 1919.

6. Stillman, F. G., and Pritchett, I. W.: *J. Exper. Med.* **29**:259, 1919.

five times neither the mother nor the child showed the bacillus of Pfeiffer in the sputum, although both had colds. In forty-four families the organism was found in both the mother and the child, both giving a history of colds. The sputum culture of the child was positive, while that of the mother was negative in twenty-three instances, though both had colds. It happened only five times that the child with rhinitis did not show the Pfeiffer bacillus while the mother did. In every one of these five instances, however, the mother gave a history of having recently had a very severe cold or an "attack of grippe." Cultures were taken from five families where neither the mother nor the child had colds and no Pfeiffer bacilli were found in a single instance. Nor were they found in any member of forty-three families where the child had a cold and the parent none. In thirty-eight families the child had rhinitis with Pfeiffer bacilli in the sputum, while the parent had no cold and her sputum cultures were negative for these bacilli. It will be seen, therefore, that the *Bacillus of Pfeiffer* is passed from the parent to the child far more frequently than from the child to the parent.

DISCUSSION

Among 1,000 cases examined for the presence of the bacillus of Pfeiffer in the sputum, the organism was found in 474; and it was not found in 526. The number of positive cases rose from 51 per cent. (114 of 221) in January, to 58 per cent. (213 of 370) in February, and fell to 36 per cent. (147 of 409) in March, paralleling the epidemic of respiratory infections which reached its peak in February and declined very decidedly during the month of March. The incidence of pneumonia cases fell from thirty-six in February to nineteen in March. Other respiratory inflammations with systemic reactions fell from fifty-two in February to twenty-three in March. The common colds, on the other hand, rose slightly in number from 114 in February to 128 in March. The percentage of respiratory cases which did not show the Pfeiffer bacillus in their sputum increased during the same period as follows: 16 per cent. of the pneumonia patients were negative in February; 33 per cent., or double as many, were negative in March. Ten per cent. of those patients with respiratory infections severe enough to give systemic reaction, but which did not develop pneumonia, were negative in February; 25 per cent. of these cases were negative in March. Thirty per cent. of the common colds were negative in February, while 44 per cent. showed the absence of the Pfeiffer bacillus from their sputum during the month of March. These results show that the bacillus of Pfeiffer was present less frequently in inflammations of the respiratory tract after the decline of the most recent epidemic of influenza in New York City.

The bacillus of Pfeiffer was present in the sputum of 74 per cent. of all the pneumonia cases studied. Eighty-five per cent. of all the cases with rhinitis and bronchitis severe enough to produce systemic reactions were positive for that organism. Fifty-three per cent. of the ordinary colds showed the bacillus; but only 11 per cent. of our controls carried it. In less than 1 per cent. of these controls who carried the bacillus of Pfeiffer was there no history of direct exposure to a case of respiratory disease from which we were able to grow the Pfeiffer bacillus. It would seem, then, that this bacillus is not a normal inhabitant of the normal respiratory tract, but that at the time when an epidemic of influenza prevails, it is present in over 50 per cent. of all cases of inflammations of any portion of the respiratory tract. Its presence in the so-called healthy carriers can, in the majority of cases, be explained by direct exposure to patients who have respiratory symptoms with the Pfeiffer bacillus in their sputum.

Bloomfield⁷ has shown that influenza bacilli quickly disappear from the normal mucous membrane of the mouth, nose and pharynx after introduction of a pure culture on the tongue, on the nasal septum behind the vestibule, or into the nasopharynx. He suggests that the presence of the Pfeiffer bacillus in so-called healthy people may result from the persistence of a chronic focus in a sinus or in a bronchus, or from contact with an acutely infected person. With this view we heartily agree.

In a previous study⁸ of 290 cases, made at the Babies' Hospital in 1909-1910, eighty-five, or 29 per cent., were found to harbor the Pfeiffer bacillus in the sputum. Among the eighty-five positive cases were nineteen who had no respiratory symptoms; but fifteen of the nineteen carriers were nurses who were in close contact with the sick children.

The incidence of the number of cases in which the sputum contained the Pfeiffer bacillus was much higher in the present study, made during the prevalence of an epidemic of influenza, than it was in 1909-1910, when no such epidemic was present. Allowing for improved technic in the present series, the increased rate of positive findings, from 29 to 47 per cent., is still striking.

Our study further shows that at a time when influenza is epidemic in a community, the Pfeiffer bacillus is very commonly present in the sputum in cases of common colds, with or without bronchitis, though those cases may be unaccompanied by general or systemic symptoms and have no relation to the clinical disease, influenza. In the three

7. Bloomfield, A. L.: *Bull. Johns Hopkins Hosp.* **31**:85, 1920.

8. Holt, L. E.: *Arch. Int. Med.* **5**:449 (March) 1910.

cases in our series in which the bacillus was found in the lungs in pure culture a diagnosis of influenzal pneumonia had been made before death.

It has been experimentally shown both in dogs⁹ and in monkeys¹⁰ that the introduction of pure cultures of Pfeiffer bacilli into the trachea may cause pneumonia. In neither case, however, has the disease produced been comparable to human influenza. Many kinds of bacteria introduced intratracheally call out an inflammatory reaction from the lung substance. Moreover, Olitsky's¹¹ work points to a filtrable virus as the probable etiological factor in epidemic influenza. The bacillus of Pfeiffer is probably an early secondary invader whose presence modifies the clinical and pathological picture.

We have brought evidence, then, that the Pfeiffer bacillus is not specific to influenza in that it is present in from 50 to 80 per cent. of cases of mild respiratory inflammations clinically not related to influenza. We have further shown that the presence of Pfeiffer's bacilli in the sputum of healthy persons can, in most cases, be traced to direct infection from another positive case, and that this bacillus does not normally inhabit the normal, human, respiratory tract. It seems to grow on any portion of the respiratory mucosa which is congested or inflamed. That it is ever the primary cause of these inflammations in human beings has not been proved; but that the local and general symptoms are influenced by its presence we believe to be true.

9. Wollstein, M., and Meltzer, S. J.: *J. Exper. Med.* **16**:126, 1912.

10. Blake, F. G., and Cecil, R. L.: *J. A. M. A.* **74**:170 (Jan. 17) 1920.

11. Olitsky, P. K., and Gates, F. L.: *J. A. M. A.* **74**: (To be published) 1920.

BULLOUS ERUPTION COMPLICATING MEASLES

FRANK C. NEFF, M.D.

KANSAS CITY, MO.

So far as I can ascertain from the literature available, no other case of this rare measles complication has been observed in this country. Henoch's¹ description of the only case he ever saw corresponds in nearly every detail with the following case:

REPORT OF CASE

S. S., girl, aged 6 years, was in a good state of nutrition and had previously been well except for an attack of influenza during the epidemic of 1918.

She became ill Oct. 31, 1919. She had a temperature of 105 F., congestion of the eyes, Koplik's spots and a cough. November 1, blotches of measles were present on the face and neck, and in twenty-four hours had extended over the entire body. By this time bullae appeared on the ears, arms and rapidly thereafter over the various other regions from 6 to 10 cm. in diameter. The eyelids became the seat of blebs so that in attempting to wash the margins of the lids the entire epidermis peeled off on contact. At the end of the second twenty-four hours of the measles, areas the size of the hand or larger became detached from the surface of the chest, abdomen, back and legs. The epidermis became wrinkled, rolled up and further denuded. The bullae were easily ruptured spontaneously or by contact with the bedclothes or hands. On the third and fourth days of the measles exanthem, the most of the body surface was involved with this grave complication, leaving much of the true skin denuded, reddened, oozing and resembling a burn. Paraffin was frequently painted over the surface with the intention of protecting the loosened epidermis, but to no purpose. In some portions of the body there appeared vesicles limited to the area of the coalescent measles lesion which had become dark or bluish and still easily distinguishable. However, the separation of the epidermis bore no relation as a rule to the site of the morbillous eruption. The eyelids became so swollen as to make it impossible to open them. The lips were swollen and covered with hemorrhagic crusts. The epidermis over the labiae majora peeled off on attempts to catheterize. The plantar surface of the feet became affected last.

The bullous content was at first macroscopically clear, later cloudy. The fluid contained pus cells, but no organisms in smears. Unfortunately, no cultures were made. The white blood count on the third day of the measles was 18,000.² The urine was never secured for examination, as catheterization was impossible, and the scanty urine voided involuntarily only once a day could not be collected.

Delirium was present throughout the disease which was markedly virulent from the first day. The temperature remained around 103.5 F., and there was no critical drop as seen usually at the end of the third day of measles. Respiratory symptoms were not pronounced; grunting, rapid or embarrassed respiration was never present, but pneumonia was regarded as possible—a physical examination of the chest being out of the question because of the raw surfaces. The child died suddenly in collapse on the fifth day of the measles. Permission for necropsy was denied.

1. Henoch, E.: *Zur Pathologie der Masern*, Berl klin Wchnschr **19**:195, 1882.

2. This case was also seen by my colleagues, Drs. Richard Sutton, dermatologist; Edwin H. Schorer and John Aull, pediatricists, and Watson Campbell, pathologist, to all of whom I am indebted for assistance.

DISCUSSION

The complicating exanthem in this case did not at any time resemble erysipelas, chickenpox or smallpox, and the lesions were far more extensive than are seen ordinarily in pemphigus. In addition to vesicles which might or might not conform to the site of the measles eruption, there were various sized bullae, some as large as a goose egg. But the most pronounced feature of the skin lesion was the far reaching separation and maceration of most of the superficial layer of the skin, which resembled an extensive burn. This gave the case a pitiable and hopeless outlook. The bullae began to appear in the first twenty-four hours of the measles rash, and thereafter appeared on various portions of the body accompanying the measles, but never preceding it. The measles eruption was no more pronounced than one sees in well marked cases, but the lesions persisted, the color became dusky or bluish. No petechiae appeared. The child was markedly toxic throughout the course of the disease.

Because of the extreme rarity of pemphigoid manifestations complicating so common a disease as measles, one can easily exclude this case from being an atypical form of measles. It seems reasonable to assume that a second exanthem developing during or shortly after the prodromal stage appeared coincidently with the eruptive stage of the measles; that its progressive or malignant nature may have been due to the well known lowered resistance to infections characteristic of measles. At a time when simple measles would have had a leukopenia, this child had a moderate leukocytosis (18,000) which may have been due to the complicating exanthem or to bronchopneumonia. One would conclude, therefore, that he had to deal here with a distinct exanthematous disease complicating or secondary to the infection of measles.

CASES FROM THE FOREIGN LITERATURE

The first cases described are the four cases of Steiner³ in 1874. He had seen 6,000 cases of measles and these four children in one family having pemphigoid lesions were the only ones of this kind he had even seen. The fact that they occurred in one household in the same epidemic of measles speaks for the contagious nature of the pemphigus. Three of these children recovered. The eruption of the vesicles appeared in the first child on the first day after the measles eruption, in the second child two days after the same, in the third child coincidentally, in the fourth child a half day before the measles eruption. New crops of the bullae appeared in the stage of desquamation. His cases were limited to bullous and pemphigoid lesions. The fatal case died in collapse.

3. Steiner: *Morbilli Bullosi Sive Pemphigoidei*, *Jahrb. f. Kinderh.* **7**:346, 1873.

Henoch,⁴ in 1882, saw a girl, aged 4 years, who on the third day of the eruption developed bullae, from hazelnut to dollar size, over the entire body. This case had practically all the characteristics of my case. Henoch states that the measles presented a darkened appearance, corresponding to what is generally called the hemorrhagic form, but after the eruption of the bullae, the skin presented the appearance of a high grade burn. The child died on the seventh day in collapse. Henoch cites the only cases he could find in literature up to that time, which were reported by Carrol in Dublin in 1868, by Gee in the *Hirsch and Virchow Jahresbericht* for 1869, Steiner's cases in 1874, and Klupfel in the *Jahresbericht* for 1875, and Loschner.⁵ The clinical picture of these cases was somewhat varied, but all patients had pemphigus; the last mentioned patient of Loschner died of pneumonia. Henoch had seen blebs in scarlet fever (miliary form) and vesicles between the lesions of variola. He was at first of the opinion that his case was a possible miliary or more highly developed case of measles, resulting from an exudation beginning under the epidermis in the course of the advanced dermatitis. This opinion he changed, as being untenable, as the bullae would then appear only where inflammation and redness of the measles exanthem is found. On the contrary, his case showed bullae more often between the morbillous lesions on the entirely unchanged skin. Steiner observed the bullae in one case appearing before the eruption, and that they continued to appear after the measles rash had faded. Henoch thinks he was dealing with a complication of acute pemphigus.

Baginsky,⁵ in 1900, reported the case of girl, aged 13 months, with bullous and later gangrenous ulceration of the skin following measles. A diplococcus was obtained in pure culture from the blood and organs. The child died in collapse nine days after the appearance of the measles.

A. Haeubler⁶ described in 1900 a case of measles combined with acute pemphigus of marked severity and the lesions extensive, but the outcome good.

John Meyer,⁷ in his thesis at the University of Bonn, in 1898, described the cases of three children in a family of four who, during a second attack of measles, developed acute pemphigus. In one case the blebs appeared before as well as after the measles exanthem. The second case occurred several days after the measles in the same epi-

4. *Jahrb. f. Kinderkrankh.* **7**: 43.

5. Baginsky: *Morbilli bullosi*, *Arch. f. Kinderh.* **28**:18, 1900.

6. Haeubler: *Ueber einen Fall von Masern, Combiniert mit Pemphigus acutus*, *Deutsch. med. Wchnschr.* **26**:533, 1900.

7. Meyer: *Ueber Complication der Masern mit Pemphigus acutus*, *Bonn*, 1898.

demic. The third case was markedly different, but the pemphigus was followed by measles after several days. The children all recovered.

Leo⁸ also described in 1898 the foregoing cases of Meyer at Bonn.

Lenier,⁹ in 1902, at the Children's Hospital, Vienna, had an opportunity to observe pemphigus in the case of four children who had measles. The first patient had blebs for two weeks, the blebs appearing eleven days after the eruption of measles. His second patient had blebs appear on the second day of the measles. The third patient began to have eruption of blebs thirteen days after the appearance of measles which lasted two days. The fourth child had the appearance of blebs twelve days after the beginning of the measles, the further observation of which was not made. All these children recovered. None of these patients had fever; the vesicles were followed by scale formation, leaving for some time bluish red spots. It is probable that these cases were entirely different from the other cases described above, and that Lenier had to deal with impetigo. At any rate, the interval before developing was long, the course afebrile, the lesions markedly differing, so that they cannot be classed as the same variety of pemphigus as is under discussion.

CONCLUSIONS

From my case and those above mentioned in the literature, it has been observed that a vesicular or bullous eruption has been rarely reported with measles. This has preceded, accompanied or followed the measles eruption. It has been found both on the site of the measles lesion and on the healthy intermediate skin. That the disease is an accidental, contagious, coincidental manifestation of the general nature of pemphigus, sometimes of virulent type, is probable. The development of a second infection of this type at any time after the beginning of the febrile onset of measles, may depend on the lowered resistance seen in measles.

8. Leo: Ueber Coincidenz von Masern und Pemphigus, *Jahrb. f. Kinderh.* **47**:70, 1898.

9. Lenier, Carl: Pemphigus contagiosus bei Masern, *Impetigo contagiosa*, *Jahrb. f. Kinderh.* **55**:316, 1902.

CLINICAL DEPARTMENT

HEMORRHAGE INTO THE SPINAL CORD AT BIRTH*

CHARLES W. BURR, M.D.

Consulting Neurologist to the Children's Hospital
PHILADELPHIA

REPORT OF CASES

CASE 1.—W. D., a boy, 4½ months old, was admitted to the service of Dr. Gittings at the Children's Hospital, Oct. 10, 1919, having had four convulsions in the preceding twelve hours, and fever and diarrhea for one week. The family history revealed nothing of interest, except that of nine brothers and sisters, three were stillborn, three died of "summer complaint," and three survive in good health. The birth was a breech presentation and in delivery the right shoulder was slightly hurt. The injury was trifling. Weight at birth was said to be 10 pounds, the same as on admission. (I suspect that the weight at birth was guessed at, not taken by scales.) The child was breast fed for one month and then was put on Mellin's food. The mother's mental level is shown by the fact that she never noticed the vitally important symptoms described below and undoubtedly present since birth. Even when shown the palsy of the child's arms and legs, she did not comprehend it.

The temperature in the rectum on admission was 102 F., and throughout the boy's illness it ran a very variable and irregular, see-saw course, sometimes going as high as 102 F. in the evening, often falling in the morning to 97 F. and sometimes even to 95 F., never remaining normal longer than a few hours.

Dr. F. H. Leavitt, who made the preliminary examination, reported the following findings: "The child lies in bed with the head held rigidly backward and rotated to the left. His appearance is typical of that seen in acute transverse cervical lesions of the spinal cord. His arms are held in the characteristic position. There is palsy of the external muscles of respiration. The pull of the diaphragm causes retraction of the lower ribs and bulging of the abdomen. There is a flaccid palsy of both legs, reflex movements in which are caused by sticking with a sharp pin. All tendon jerks are abolished in both legs. Stroking the sole of either foot causes fanning of all the toes but no extension. (Extension is normal at his age.) When fretful, his cry is weak because of the palsy of the chest muscles. Deglutition is normal. Both pupils react to light; the left is widely dilated, the right normal in size. The child probably is too young to accommodate. (At what age a healthy child begins to accommodate is still a disputed question.) There is anesthesia of the skin and deeper tissues of both legs and trunk."

Physical Examination.—The general examination revealed the following. There were crepitant râles throughout the chest. The heart was normal. There was no deformity of the spine; no pain on pressure along its course, and a roentgenogram revealed nothing abnormal. The fluid obtained by lumbar puncture came out under slight pressure, was clear at first and at the end slightly tinged with blood. The cell count was ten and the fluid was free from bacteria. The urine was normal; the blood Wassermann and the von Pirquet skin reaction were negative. There was no leukocytosis. The clinical diagnosis was

* Read before the Philadelphia Pediatric Society, March 9, 1920.

lobar pneumonia and hematomyelia from birth injury. Notwithstanding the mother's statement that she had noticed nothing wrong with the child till a few days before coming to the hospital, the history of the birth and the answers given by her to questions as to how long the arms and legs had been useless (i. e., palsied) made the diagnosis of birth palsy positive. The patient died Oct. 19, 1919.

Necropsy Report.—At the necropsy, made by Dr. G. M. Mitchell, there was found a right-sided lobar pneumonia with complete consolidation of the lower lobe, middle lobe and lower half of the upper lobe. The left lower lobe behind was congested. (It is probable that the palsy of the chest walls was an important mechanical predisposing cause of the pneumonia, increasing susceptibility to bacterial infection of the lung.) There was no evidence of any injury to the vertebrae nor were there any signs of an old extradural hemorrhage. The spinal cord, with the membranes, formed, from the fourth cervical nerve root to the first dorsal, a soft, apparently fibrous band; above and below this area both cord and membranes were grossly normal. The dura nowhere showed gross disease on the other surface (Fig. 1). The brain was not removed. There were no old or recent hemorrhages in any of the abdominal or thoracic viscera.

Microscopic examination of the spinal cord by Dr. A. J. Smith showed the dura mater in the narrowed area to be the seat of a fibrous thickening and induration which was more marked posteriorly than anteriorly. The fibrous

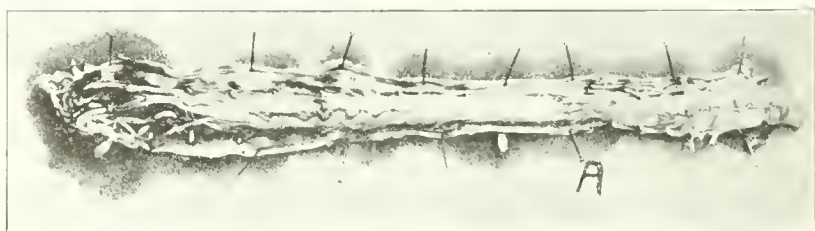


Fig. 1.—Spinal cord from Case 1. A indicates the level of hemorrhage.

stroma contained more young cellular elements than elsewhere and there were a number of blood vessels with rather swollen endothelial lining and rather cellularized walls. The dura mater here, too, was adherent to the pia mater which was thickened. On cross section of the cord the gray matter could not be recognized, there were no multipolar cells, and only a few patches of degenerated white matter were seen. There was no normal white matter. Practically, the cord at this level was completely destroyed. The nerve roots outside the cord, and arising above the level of the section, stained well and normally. There was ascending degeneration above the area of destruction and descending degeneration below. There was no disease of the lumbar swelling, barring the descending degeneration.

CASE 2.—J. D., an Italian boy, 3 months old, was admitted to the Children's Hospital, July 22, 1919, with a palsy of both legs which had existed since birth. His parents and three other children are living and well. His birth was by breech presentation at full term and, according to the mother, "the doctor had pulled too hard." He almost died at birth and was completely palsied from the neck down. When two months old he had one slight convulsion. Dr. Leavitt referred him to my clinic at the Orthopedic Hospital.

Physical Examination.—Examination revealed the following: There was total and complete flaccid palsy of both legs. All deep reflexes and the plantar jerk were absent. The heart heat was 140. In the back, in the region of the fourth to sixth cervical vertebrae there was a marked valleylike depression.

At rest the forearms were flexed on the arms, the hands extended at the wrist, and the middle phalanges flexed. The shoulders were somewhat extended. The lower right facial movements were more marked than the left. The fontanelles were open. The head was hyperextended. There was some voluntary movement of the shoulders, less of the arms, none of the forearms and hands. Breathing was diaphragmatic. The chest was drawn in and the belly ballooned. He moved the tongue well. There was complete anesthesia in the legs and trunk.

He was returned to the Children's Hospital. No new symptoms appeared. Breathing was diaphragmatic. The abdominal muscles were toneless and palsied. The palsy of the legs continued flaccid with absent knee jerk, Achilles jerk and plantar reflex. The pupils responded to light but there was no accommodation. The roentgenogram of the spine showed no disease or deformity of the bones. (The depression mentioned above was muscular, not bony.) The child died Sept. 9, 1919. A necropsy was refused.

DISCUSSION

There is not a very large literature on the subject and in America almost no attention has been paid to it. Herbert R. Spencer¹ reported a series of 130 autopsies on fresh, mostly stillborn fetuses in a study of visceral hemorrhages in stillborn children. The spinal cord was examined in forty-four cases. "In no case was there separation of the vertebrae." (I interpret this to mean that there was no evidence of injury to the spine.) "In 5 cases the cord, membranes, and surrounding cellular tissue were normal; in none of these was traction employed. Three were apparently natural vertex deliveries; in one case version was employed, followed by natural delivery; in one case the forceps was employed to hold the head in the pelvic brim, but not to deliver." In eighteen cases there was congestion or edema of the spinal cord. (The personal equation plays a large part with everyone in diagnosing edema and congestion at necropsy.) In thirty cases there was hemorrhage somewhere within the spinal canal. In six cases it was within the spinal cord; in one case into the whole thickness of the cord; in four cases into the anterior cornua, in one case into Goll's column in the lumbar region. Six were naturally delivered cephalic cases; thirteen were breech or footling cases; four were delivered artificially by forceps; one was delivered by cephalotripsy. In one case no record was kept of the method of delivery. Spencer concludes that "spinal hemorrhage is greatly favored by the presentation of the lower extremity." This is, he states, "probably due partly to the greater compression undergone by the soft parts, and to the consequent driving of the blood to the central organs, and partly to traction sometimes employed."

Discussing the causes of visceral hemorrhage in stillborn children, Spencer states: "The hemorrhage must have as cause one or more of three factors: (1) Thinness and weakness of the wall of the blood

1. *Tr. Obstetrical Soc. Lond.* **33**:203, 1892.

vessels. (2) Alteration of the blood rendering it more prone to escape. (3) Increased blood pressure from (a) asphyxia or other vasomotor disturbance or from pressure on veins; (b) squeezing of blood into some parts of the body in the act of birth; (c) external violence rupturing the vessels at the point pressed upon." He thinks that syphilitic disease of the blood vessels plays little part in the production of hemorrhages. He regards "the normal delicacy of the fetal vessels as the one essential feature in the causation of hemorrhage." In his view, asphyxia plays little or no part, except that, combined with other causes, it renders hemorrhage more frequent. "Mechanical squeezing of blood into some parts of the body during the act of birth is probably a frequent cause of hemorrhage." External violence may rupture a vessel, as in a case of apoplexy of the lung produced by pressure of the rigid cervix on the child's thorax.

Drs. A. H. Davisson and D. J. McCarthy² report a case of transverse myelitis in a new-born infant. The child could move its head and arms, but the rest of the body remained an inert mass. Sensibility was surely lost up to the level of the xiphoid cartilage. The arm reflexes were present. The plantar, knee and abdominal jerks were absent. At necropsy, the cervical and highest dorsal cord and the lumbar enlargement seemed to be normal. There was flattening from the second to the eleventh dorsal. The case is most interesting from the point of view of physiology, namely, as regards the much disputed question as to whether total transverse lesion of the cord above the lumbar swelling causes abolition or increase in intensity of the reflexes of the legs. In this case they were absent. The deep reflexes were absent in both my cases (normally, the knee jerk is present from birth; the abdominal skin reflex appears later), and there was undoubtedly a total transverse cervical lesion in both. This is strong evidence, but the cerebrospinal apparatus is not complete at birth, the reflexes appear at different ages, and in the case of the plantar jerk what is normal in babyhood is pathologic later, and it may be that the effect of a total transverse lesion is not the same then as in adult life.

In my first case, the necropsy proves that there was a hemorrhage within the cord and a subsequent myelitis. The second case clinically so resembles the first that it is safe to conclude it had the same cause.

The fact that in thirty out of forty-four of Spencer's cases of stillbirth (or death almost immediately after birth) there were hemorrhages within the spinal canal, while it was within the cord itself in only six, is of great interest. It would be interesting to know in what proportion of hemorrhages within the cord at birth there are hemorrhages elsewhere in the body, because when hemorrhages are present

2. Phila. M. J. **11**:357 (Feb. 21) 1903.

elsewhere, it is safe to conclude that the spinal hemorrhage was not caused by direct trauma to the cord, nor the consequence of a vertebral dislocation, but that it was the result of asphyxia or squeezing of an excess of blood into the organ, thus putting such pressure on the walls of the vessels as to rupture them. The explanation of the cause of spinal hemorrhage is complicated by the fact that it seems fairly well proven, in the adult at any rate, that a momentary dislocation of the vertebrae may occur, and if it causes death, the necropsy may not reveal any injury to the ligaments, but only a crushed cord. This is an accident not likely to happen, however, in a breech presentation. In the case here reported, notwithstanding the careful examination made, I am still uncertain as to the immediate cause of the hemorrhage. There were signs of inflammation in the dura mater which could not have, or one would not expect them to have, resulted from a hemorrhage spontaneously arising within the cord, from squeezing of an excess of blood into the vessels. On the other hand, there was no evidence that the dura mater had sustained any direct injury, such as a bruise or tear by spinal dislocation, nor did the spinal ligaments show any injury. Balancing all the evidence, I incline to the belief that the hemorrhage was spontaneous and not caused by direct violence, but by rupture of over-full vessels from pressure on the soft parts during birth.

PROGRESS IN PEDIATRICS

VON PIQUET'S FEEDING SYSTEM

HAROLD K. FABER, M.D.

Associate Professor of Medicine (Pediatrics), Leland Stanford Junior
University Medical School

SAN FRANCISCO

Of the many innovations and ingenuities for which the war was responsible, none are more interesting than those which were devised and forced into practice in the attempt adequately to feed the peoples of belligerent countries on a reduced food supply. There have recently come to this country some accounts of the system of feeding, intended primarily for children in institutions but later given a much wider application, which von Pirquet introduced in Vienna early in the war. Von Pirquet has published a book¹ expounding the system, which is not yet available here; his associate, Schick, has, however, given us a comprehensive review² of the work, and from this the present account is taken. A review of von Pirquet's original articles has been published elsewhere,³ and a short account of his experiences with the system is given by von Gröber.⁴ The system possesses much matter of interest to students of nutrition as an ingenious and novel attempt to rearrange the data of nutritional science with the purpose of obtaining popular interest and comprehension for scientific feeding, and of making the fullest possible utilization of available foods while obtaining for each individual his just quota of food and eliminating waste. To these ends a thoroughgoing reform of current practice in feeding was attempted not only in institutions but in the home, in restaurants, in community kitchens and, indeed, wherever groups of people were fed.

In the Central Empires the necessity of economy with food was, of course, felt soon after the outbreak of hostilities because imports of food were cut off so early, and these countries customarily depended on foreign sources for from 5 to 15 per cent. of their food supply. The shortage, as it applied to the civil population, was aggravated by

1. Von Pirquet, C. F.: *System der Ernährung*, Berlin, Julius Springer, 1917.

2. Schick, B.: *Das v. Pirquetsche System der Ernährung*, *Ergebn. d. Inn. Med. u. Kinderh.* **16**:384, 1919.

3. *Monatsch. f. Kinderh.* **16**:4, 1919.

4. *Ztschr. f. Kinderh. (Sonderheft)* **18**:297, 1918.

the necessity of feeding the armies a larger per capita ration than had been required by the same individuals during times of peace. Increased production was impossible for reasons which it would be superfluous to state here; indeed, there was a progressively diminishing production. An equitable distribution of food was attempted but failed because of the refusal of the peasants to cooperate. The only available means of securing adequate food supplies for the urban populace consisted, therefore, in eliminating waste and in utilizing every available food in the most economical manner compatible with maintenance of life and working power.

It was felt that of all the classes of the population none, with the exception of the armies, had a greater claim to adequate nutrition than the infants and children. It was in the effort to meet this claim that von Pirquet, of Vienna, cast about for a plan of scientific food apportionment which would enlist popular support and hence be put into general practice. He felt that there were serious objections to the caloric system which robbed it, practically speaking, of any prospect of general adoption. The goal he aimed at was a system which would first of all be accepted and used on the merits of its own appeal by cooks and housewives generally. Given this psychologic acceptability, the primary purposes of ensuring a qualitatively and quantitatively adequate food supply to the individual, of eliminating waste and of making use of the foods which should be actually available, could be attained.

Von Pirquet's objection to the use of the calorie as the unit of food value lay largely in the considerations of popular psychology. His idea was that the conception of food units as heat units is so abstract that not only the laity but most professional men as well fail to connect it with reality and for practical purposes search for a more direct means of comparison. Many physicians, for instance, compare foods with the egg as a unit of value. Von Pirquet believed that a direct comparison unit of this sort would win general acceptance by its direct imaginative appeal. Thus the first step in popular education in the scientific use of food would be gained. Milk, as the first and only specifically physiological food, was selected as his standard of comparison. More exactly, he compares all foods in actually utilizable caloric value to a breast milk of the composition: 3.7 per cent. fat, 6.7 per cent. sugar and 1.7 per cent. protein. Cow's milk of the composition: 3.7 per cent. fat, 5.0 per cent. sugar and 3.3 per cent. protein, has the same value. This standard milk has a physiologic (utilizable) caloric value of 667 large calories per liter. The unit of food value in von Pirquet's terminology is the "nem" (*Nahrungs-Einheit-Menge*).

representing the food (caloric) value of 1 gram of standard milk. A nomenclature for the decimal fractions and multiples is provided as follows:

0.001	nem = 1 millinem (mn)
0.01	nem = 1 centinem (cn)
0.1	nem = 1 decinem (dn)
10.0	nem = 1 dekanem (dkn)
100.0	nem = 1 hektionem (hn)
1000.0	nem = 1 kilonem (kn)
1000	kilonem = 1 tonnenem (tn)

Of these, the decinem, nem and hektionem are the ones most commonly used in practice.

Von Pirquet has worked out an elaborate nomenclature for expressing various interrelationships between body measurements, combining abbreviative roots to form a rather startling series of neologisms.

Si: sitting height. Sta: standing height. Be: standing height minus sitting height (leg length). Le: distance from tip of elbow to most distant finger tip. Fe: length of foot from heel to tip of first toe. Au: circumference of arm just above elbow joint. Ku: greatest circumference of head, fronto-occipital. Su: circumference of thigh just above knee. Bru: mean chest circumference at level of ensiform process. Ke: head length, forehead to occiput. Kei: greatest width of head. Gi: body weight without clothes (net weight). Ge: tenfold weight.

Du: divided by; qua: square, or second power; ku: cube, or third power; 1: root; lei: second, or square root; li: third, or cube root.

The nomenclature is best explained by a few examples. The relationship between length of the lower extremities, and sitting height is called Bedusi (*Be*, leg length; *du*, divided by; *Si*, sitting height). Gili is the cube root of body weight. Staku is the cube of the standing height. Siqua is the square of the sitting height. Stakudugi is the cube of the standing height divided by body weight. Gelidusi is the cube root of the tenfold weight divided by the sitting height. Geliqua is the square of the cube root of the tenfold weight.

The names most commonly used appear to be Siqua, Gelidusi, Geliqua and Gili.

Von Pirquet's next step was to provide a basis for conveniently estimating the food requirements of the individual. Here the demand was for a measurement which could be made easily and with reasonable accuracy with the simplest apparatus, and which would bear a more or less constant relation to the food requirements of the body. Only two methods met these specifications—the measurement of body weight, and some linear measurement of the body. Von Pirquet goes into an exhaustive discussion of the relative merits of the two methods, for the details of which the reader is referred to the original. In general, it may be said that the energy exchange may be expressed as a

function of the surface area not only of the skin, but of all internal surfaces — of the intestines, blood vessels, serous cavities and, in the last analysis, of every cell of the body. Heretofore the energy exchange has been brought into relationship with the skin area only, as determined by the Vierordt-Meeh formula or one of its modifications, from the body weight. Von Pirquet asserts that the formula may be applied by the use of a different constant, to the determination of the total surface areas of the body, and that the result then gives an accurate index of the total energy exchange. The use of the formula, however, necessarily involves the derivation of a cube root in every case, and for everyday work this is quite impracticable.

In casting about for a simpler index, von Pirquet conceived the idea that intestinal area, as representing the surface which governs the amount of food absorbed, would afford a logical basis for estimation of food requirements. In calculating intestinal area, he used an observation made by Henning in 1881, that the length of the intestine equals the sitting height multiplied by ten, and a deduction from various observations on intestinal volume that the width of the intestine is equal to one-tenth of the sitting height. The latter figure is plainly arrived at by guess-work, and must be regarded as largely an arbitrary value since the width of the intestine will depend on the degree of tension exerted at the time of measuring it. Accepting these figures,

the area of the intestine can be expressed as $10 \text{ Si} \times \frac{\text{Si}}{10}$, or Si^2 , a

value which von Pirquet terms "Siqua" and uses extensively in his system. This ratio is constant throughout childhood and maturity.

Von Pirquet had previously determined in his series of studies on development that there is in normally developed and normally nourished individuals a constant relationship between sitting height and weight, expressed by the formula, $\text{Ge} = \text{Si}^3$, from which may be deduced the secondary formula, $\text{Ge}^{\frac{1}{3}} = \text{Si}$, when Ge is $10 \times$ weight.

5. Von Pirquet states in another place that in adults with powerful musculature and in fat infants Gelidusi (the cube root of ten times the body weight, divided by the sitting height) equals 100. The average growing child has a Gelidusi of about 94, and in extreme emaciation the figure may sink as low as 81. There are certain minor inaccuracies and disagreements in the original. For instance, Gelidusi, as employed by von Pirquet, really equals the cube root of the tenfold body weight in grams, divided by the sitting height in centimeters, multiplied by 100. Further, it is stated, as quoted in the preceding paragraph, that in normally developed and nourished persons, $\text{Ge}^{\frac{1}{3}} = \text{Si}$. From this equation may be derived $\text{Ge}^{\frac{1}{3}} = \text{Si}$, and hence $\frac{\text{Ge}^{\frac{1}{3}}}{\text{Si}} = 1$, which is equivalent to a

Gelidusi of 100. My own observations lead me to the conclusion that Gelidusi equals 100 only in exceptionally fat children. Gelidusi is much used by von Pirquet and his associates as an index of the state of nutrition of the individual patient.

Since the two-thirds power of the weight has a direct relationship with surface areas of the body, it is evident that the sitting height also has a similar relationship which is capable of mathematical expression. Working from two different starting points, therefore, von Pirquet arrived at the same value — the square of the sitting height — as a measure of food requirements and the energy exchange of the body. The sitting height is easily measured with the simplest apparatus, and its application involves squaring only, instead of squaring and cube root derivation, as in the case of weight. The imaginative nexus between the figure so arrived at and the intestinal area is given as an additional argument for the popularity of the system. Von Pirquet considers at length the objections which may be offered to his theories, particularly as to the slight basis in fact for certain of his assumptions; he answers the objections largely with the statement that his assumptions meet the pragmatic test satisfactorily, since they lead to successful results in practice.

The fundamental question of food requirements and the means of estimating them are next taken up. The output of heat by the body — as determined by direct calorimetric methods — is rejected as an unreliable measure of the working needs. "Such conditions" — those of direct calorimetry — "are only exceptionally met with in life, as for instance, in the bedridden invalid. In normal times we do not fast but are accustomed to satisfy several times a day the impulse to eat. The active, growing child and the man doing bodily work show quite different combustion processes than in the physiologic experiments of Rubner. The working man, thinks von Pirquet, does no work for the purpose of keeping his temperature from falling. On the contrary, he must throw off the excess of formed heat by sweating. The heat formed by the body is not the main goal of the life process but its side-product." Food needs are best measured — and in a large series of observations, most accurately — by the actual amounts of food spontaneously ingested under the various conditions of life. Using this method, von Pirquet and his associates measured the amount of food taken without limitation by an unstated number of individuals of various ages for 30,000 trial days, deducing from the figures so obtained an estimate of minimum, optimum and maximum intake values. These values they proceeded to correlate with the sitting height. They give the following definitions:

The minimum intake is that quantity of food which just covers the healthy body's needs for so-called internal work. It is the amount of food required by an individual during complete rest in bed to maintain a constant body weight.

The optimum intake is the least amount of food which will permit (a) an infant to perform his usual activities and to gain in weight and to grow at the normal rate; and (b) an adult to perform his customary work while maintaining a constant weight.

The maximum intake is the greatest amount of food which the intestinal canal can handle without injury.

The optimum varies greatly with age and occupation. In calculating the daily ration, we must cover, first of all, the needs for internal work (minimum intake) and add thereto amounts of food sufficient to cover the needs for all other activities and functions carried on by the individual. In conditions of disease the optimum may equal the minimum. On the other hand, when the most arduous work is done, or in the case of wet nurses who have to nurse both their own and another infant, the optimum may reach the maximum. As a rule, of course, the optimum stands somewhere between minimum and maximum.

The minimum quota as related to the sitting height is determined from the following formula:

$$0.3 \text{ nem} \times \text{Si}^2 \text{ (3 decinem Siqua)}$$

The food requirements of the individual are determined by additions to this minimum of the quotas for growth, fat deposit (Fettansatz), and muscular activity according to his conditions of life, as follows:

Growth	0.1	n Si ²
Fat deposit.....	0.1-0.2	n Si
Muscular activity:		
Light sedentary occupation.....	0.1	n Si
Muscular activity, early infancy; more active sedentary occupation	0.2	n Si
Light manual standing work; active playing (children)	0.2	n Si
Hard manual work.....	0.3-0.7	n Si
The maximum is stated to be 4.0 n Si.		

In explanation of the method of practical application, the following examples are given:

Infant in first half year:

Minimum	0.3 n Si
Growth	0.1
Fat deposit.....	0.1-0.2
Total	0.5-0.6 n Si

The food needs of this infant in terms of grams of standard breast milk will, therefore, equal the square of the sitting height in centimeters multiplied by 0.5-0.6. If the sitting height is 35 cm., the requirement is $35^2 \times 0.5$ (0.6) = 1225 \times 0.5 (0.6) = 612.5 (735) gm. standard breast milk.

Infant in second year:

Minimum	0.3 n Si ²
Growth	0.1
Muscular activity, according to degree.....	0.2-0.4
Total	0.6-0.8 n Si ²

Adult in light sedentary occupation:

Minimum	0.3 n Si ²
Muscular activity.....	0.1
Total	0.4 n Si ²

Adult in standing occupation, moderately severe:

Minimum	0.3 n Si ²
Muscular activity.....	0.2
Total	0.5 n Si ²

Adult in very heavy manual work:

Minimum	0.3 n Si ²
Muscular activity.....	0.7
Total	1.0 n Si ²

If the last mentioned individual has a sitting height of 90 cm. his food requirement in terms of standard milk will be

$$90^2 \times 1.0 = 8100 \text{ gm. milk (or 8100 nem, or 81 hektonem)}^6$$

It is interesting to note that, according to von Pirquet, a child in the second year, because of the greatly increased muscular activity, requires more food, relative to his sitting height, than an infant in the first half year, a time when, according to opinions generally held, the caloric needs per unit body weight are greatest. Another statement of interest is that during puberty the requirement is 0.7-0.8 n Si², a figure which is comparable with that of an adult performing hard manual work.

While there is admittedly a large amount of empiricism in the methods by which the standards have been established, there is a readily available check on their accuracy in the maintenance of normal growth in infants and of constant body weight in adults. This check has been freely applied and the claims for accuracy thus substantiated by von Pirquet and his associates.

The system was, of course, intended to be given its widest application in group feeding. Up to the present it has been used in hospitals, feeding clinics, sanatoria and community kitchens mainly, but is beginning (1918) to be used in private homes as well. Von Pirquet hopes

6. While the authors do not use the calorie at all, it will be noted that two-thirds of the nem value equals the caloric value.

that eventually it will be used also in large industrial establishments and perhaps in armies.

To make group feeding by the new method easier von Pirquet called for a revision of cooking books so that the recipes will specify ingredients in unit quantities, preferably in hektogram (hn). In several clinics and hospitals in Vienna a revision of this sort has been made. Lacking such standard recipes, the quantities at present specified can be calculated in nem units. The accompanying table will give an idea of the values for some common foods, together with the protein content, which is also taken into account.

TABLE SHOWING "NEM" CONTENT OF FOODS

Nem per Gm.	As Purchased *	As Prepared in Kitchen	Gm. per 100
13.3 (40/3)	Beef suet 0, lard 0, oils 0		7.5
12	Butter 0, margarine 0		8.5
11	Bone marrow 5		9.0
10	Bacon H		10.0
9	Shelled nuts H		11.0
8	Sweet almonds 1		12.5
0.7 (20/3)	Cracklings 1, fat sausage 1, whole milk powder 2		12.5
6	Sugar 0, cocoa powder 1, chocolate 0		17.0
5	Ham 3, smoked meat 3, fresh meat (fat) 2, skin milk cheese 4, whole milk cheese 3, sweetened condensed milk 1, legume flour 2, grain flour 1, dry flour paste preparations 1, zwieback 1, rice 1, starch flour 0, honey 0, syrup 0, skin milk powder 4, dried haddock 7	Pastries 1	20.0
4	Fish roe 4, blood sausage 1, dried legumes 2, fine wheat bread 1, dried dates H		20.0
3 (10/3)	Unsweetened condensed milk 2, graham bread 1, dried vegetables H-3, mushrooms 3	Marmalade 0	20.0
3	Black bread 1, sardines 5, smoked sprats 4	Light pastries 1	20.0
2.5 (10/4)	Fresh meat (medium fat) 4, fresh fish (fat) 4, eggs 3, chestnuts 1	Prepared meats 6	40.0
2	Fresh meat (lean) 6, fresh liver and kidneys 5	Double food**: corn meal mush 1, prepared vegetables: legumes 2, spinach 1, cabbage H, rice H	20.0
1.5 (3/2)	Calf brains 3, fresh herring 7	Prepared fish 1	27.0
1.25 (5/4)	Lungs, blood 7, fresh fish (lean) 7, potatoes H, fresh haddock 7		80.0
1	Woman's milk 1, cow's milk 2, green peas 2, wine grapes H, sweet grapes H, bananas H, figs H	Equivalent foods**: Prepared vegetables: potatoes H, milk dishes 1, thick soup 1	100.0
0.67 (2/3)	Fresh fruit H, fruit juices 0, celery 1		15.0
0.5 (1/2)	Centrifugalized skim milk 4, string beans 2, carrots 1, fresh onions 1	Half foods**: Thin soup 1	20.0
0.4 (4/10)	Fresh spinach 3, soup greens 1, cabbage and cauliflower 2, turnips 1, fresh mushrooms 3		25.0
0.25 (1/4)	Asparagus 1, tomatoes 2		40.0
0.2 (2/10)	Lettuce 2, cucumbers 2		50.0
0.1 (1/10)		Ment brot	100.0

* The number to the right of the food is the protein value; 0, no protein; H, half. The unit of protein is 0.1 nem per gm., the value in woman's milk.

** Double foods, equivalent foods and half foods contain respectively twice, the same and half the nem values per unit as woman's milk.

Wherever there is a group to be fed by the new system, the members are measured and divided into subgroups, according to sitting height, of individuals having the same food requirement. In practice the food requirements of the individuals are determined and reduced to the nearest 5 hn. Individuals requiring 10, 15, 20, 25, 30, 35 hn, etc.,

are placed in corresponding groups designated I, Ia, II, IIa, III, IIIa, etc. The physician or director of the service then determines the total number of food units required daily for the group. Thus, if there are fifty-five children, the calculation will be made somewhat as follows:

Group II, 1 child.....	$1 \times 20 \text{ hn} = 20 \text{ hn}$
Group IIa, 20 children.....	$20 \times 25 \text{ hn} = 500 \text{ hn}$
Group III, 16 children.....	$16 \times 30 \text{ hn} = 480 \text{ hn}$
Group IIIa, 11 children.....	$11 \times 35 \text{ hn} = 385 \text{ hn}$
Group IV, 7 children.....	$7 \times 40 \text{ hn} = 280 \text{ hn}$
Total	<u>1,665 hn</u>

The exact amount of food required daily is thus found and the dietitian orders accordingly. The dietitian or cook makes up the menu which is varied according to desire, expense and the foods actually available.

In serving the meals at one of the clinics, the children were seated at benches or tables which served to mark off the different feeding groups. Liquid foods were measured out in calibrated ladles. Solid foods were weighed en bloc as prepared and then divided in aliquot portions. The different groups simply received different amounts of the same dishes. The result was that each child received the exact amount of food he required and that, because of the accurate predetermination of the whole amount needed for the group there was no waste in the kitchen.

As regards infant feeding, von Pirquet has worked out a simplified system of milk modification, involving dilutions and additions with what he calls "equivalent" and "double" foods. An equivalent food contains the same number of food units per unit volume as the standard milk, and a double food, twice the number. An example of the former—and the one most commonly used—is 17 per cent. cane sugar solution. Dilutions of milk with this solution in any proportion have the same food value per unit volume as milk itself, so that no further calculations are necessary than in the case of undiluted milk. Gruels are made up to twice the food value of milk and are the common type of double food. When a gruel feeding is substituted for a milk feeding it is therefore given in half the quantity, and no further calculation is necessary. As an example of how simply the plan works out, the case of an infant 4 months old, with a sitting height of 38 cm. is considered. The food requirement is 0.5 n Si^2 , or 0.5×38^2 , or 720 n. The clinician decides that the child can take a half-and-half mixture, which is made by diluting 360 c.c. of milk with 360 c.c. of a 17 per cent. cane sugar solution. The mixture is divided into six bottles of 120 c.c. If it is desired to substitute a gruel feeding, 60 c.c. of gruel is the

equivalent amount. The correct amount of meat, vegetables, cereals, etc., to be added to meet the requirement when the change to a general diet is made can be easily found from the table of food values.

The question of protein requirements is discussed and a novel method of estimating them presented. Arguing from the protein content of breast milk, von Pirquet says that if man at the time of most intense growth requires only 10 per cent. of his food values in the form of protein, this quota should be enough—at least as a minimum—for any later period of life. He believes that the function of protein is not only to replace worn-out tissue and to supply material for new tissue, but also to make possible an adequate supply of digestive ferments which must stand in close relationship to the amount of food ingested. He, therefore, favors the expression of protein needs as a fraction of the total food requirement, rather than as an absolute quantity. It seems probable from the fact that in animals the minimum has been estimated as 5 per cent., that the human minimum is somewhat less than 10 per cent. of the total food intake. The comparison of the protein requirement calculated on the basis of 10 per cent. of the total food with the figures given by other investigators is interesting.

The average adult requires approximately 3,500 nem per day. His protein requirement, then, would be 350 n. Since protein has a value of 6 n per gram, the protein requirement would be about 60 gm. — far less than Voit's average figure of 115 gm., nearly that of the American investigators and considerably more than Hindhede's minimum figure of 39 gm. per day.⁷

While allowing a moderate increase for those engaged in hard manual labor (up to a maximum of 20 per cent.) the use of protein as a fuel food is strongly condemned on grounds both of health and of economy, and is compared to the use of fine furniture or violins in building fires.

Fat, in von Pirquet's opinion, is not a fundamentally essential article of diet, except as a requisite in cooking technic. It is purely a fuel food with a high value per unit volume, elaborated by Nature for the sake of compactness. It can be replaced entirely by carbohydrates, without harm to the organism.

The following quotation is of interest: "It has often been pointed out that while there is no fat minimum, the exclusion of fat would withdraw substances (lipoids, vitamins) which are important to life.

7. Calculating from the average figures for mature breast milk published by Holt, Courtney and Fales: fat, 3.27 per cent.; sugar, 7.50 per cent.; protein, 1.15 per cent.; protein supplies only 7.15 per cent. of the calories.

Von Pirquet could see nothing in practice which really corresponded with this theoretical consideration. The objection is at present still a theoretical one, but certainly requires further proof." And the following remarkable experiment is recorded: "The attempt was continuously successful to feed infants from birth for months (the experiment lasted about twelve months) with centrifugalized skim milk, without demonstrable disturbance in a child which could in the slightest degree be related to the food. The fat was replaced by equivalent amounts of cane sugar. Even as regards the lessening of immunity to infectious diseases there was nothing to be noted."

INDEX TO VOLUME 19

	PAGE
Abnormalities, roentgen-ray demonstration of abnormalities of gastro-intestinal tract in children; C. G. Kerley.....	277
Acetone, elimination of acetone bodies during infectious fevers; B. S. Veeder and M. R. Johnston.....	141
Achondroplasia, study of achondroplasia, introducing a new symptom—wedge-shaped vertebra; T. F. Wheeldon.....	1
Allergy in infants and children; O. M. Schloss.....	433
Anaphylaxis, review of literature of past five years on anaphylaxis and related phenomena; A. R. Cunningham.....	392
Anatomy, physiology and pathology of infancy and childhood, recent work in; J. B. Holmes.....	418
Arthritis deformans, etiology of, in children; A. H. Byfield.....	87
Athrepsia, results of some experimental work with sodium cacodylate on athreptic infants; F. S. Clarke and A. Dow.....	260
Atrophic infants, dextrose tolerance in; P. M. Mattill, K. M. Mayer and L. W. Sauer.....	42
Bacillus of Pfeiffer in inflammations of respiratory tract in children. M. Wollstein and R. C. Spence.....	459
Baker, H. M.: Incidence of protein sensitization in normal child.....	114
Blood, nitrogenous and sugar content of, of new-born; J. P. Sedgwick and M. R. Ziegler.....	429
Blood, studies with new method for determining coagulation time of blood in new-born; F. C. Rodda.....	269
Boorstein, S. W.: Treatment of birth fractures at Fordham Hospital.....	375
Brown, A.: Effect of intravenous injections of calcium in tetany and influence of cod liver oil and phosphorus in retention of calcium in blood...	413
Buffalo, food value of milk of water buffalo; W. W. Cadbury.....	38
Bullous eruption complicating measles; F. C. Neff.....	469
Burr, C. W.: Hemorrhage into spinal cord at birth	473
Byfield, A. H.: Antineuritic and growth stimulating properties of orange juice	349
Byfield, A. H.: Etiology of arthritis deformans in children.....	87
Cadbury, W. W.: Food value of milk of water buffalo.....	38
Calcium, effect of intravenous injections of calcium in tetany and influence of cod liver oil and phosphorus in retention of calcium in blood; A. Brown, I. F. MacLachlan and R. Simpson.....	413
Calcium metabolism of infants and young children and relation of calcium to fat excretion in stools: children taking a mixed diet. L. T. Holt, A. M. Courtney and H. L. Fales.....	291

INDEX TO VOLUME 19

PAGE

Calcium metabolism of infants and young children, and relation of calcium to fat excretion in stools; infants taking modification of cow's milk; L. E. Holt, A. M. Courtney and H. L. Fales.....	97
Calhoun, H.: Résumé on circulatory system; review of literature of 1917, 1918 and 1919.....	62
Chondrodysplasia; multiple cartilaginous exostoses, report of cases; H. L. Dwyer	189
Circulatory system, résumé on; review of literature of 1917, 1918, 1919; H. Calhoun	62
Clarke, F. S.: Results of some experimental work with sodium cacodylate on athreptic infants	260
Cod liver oil, effect of intravenous injections of calcium in tetany and influence of cod liver oil and phosphorus in retention of calcium in blood; A. Brown, I. E. MacLachlan and R. Simpson.....	413
Colon, dilatation of, in children. A. E. Meyers.....	167
Courtney, A. M.: Calcium metabolism of infants and young children and relation of calcium to fat excretion in stools; children taking a mixed diet	201
Courtney, A. M.: Calcium metabolism of infants and young children and relation of calcium to fat excretion in stools; infants taking a modification of cow's milk.....	97
Craniotabes and beading of ribs as signs of rachitis; H. Schwarz.....	384
Cunningham, A. R.: Review of literature of past five years on anaphylaxis and related phenomena	392
Daniels, A. L.: Antineuritic and growth stimulating properties of orange juice	349
DeBuys, L. R.: Case of anomaly of diaphragm with herniation into thorax of certain viscera resulting in gastric and intestinal obstruction.....	55
Dehydrated infants, fluid injections in; S. McLean and C. A. Lang.....	359
Dextrose tolerance in atrophic infants; P. M. Mattill, K. M. Mayer and L. W. Sauer.....	42
Diaphragm, anomaly of, with herniation into thorax of certain viscera resulting in gastric and intestinal obstruction; L. R. DeBuys.....	55
Dow, A.: Results of some experimental work with sodium cacodylate on athreptic infants	260
Dwyer, H. L.: Chondrodysplasia; multiple cartilaginous exostoses, report of cases	189
Emphysema, subcutaneous, in an infant three days old; H. K. Faber....	388
Esophagus, congenital stricture of, report of two cases; J. L. Morse.....	144
Exostoses, multiple cartilaginous exostoses, report of cases; H. L. Dwyer	189
Eyster, J. A. E.: Auriculoventricular heart block in children, with report of case	131
Faber, H. K.: Subcutaneous emphysema in an infant three days old.....	388
Fales, H. L.: Calcium metabolism of infants and young children and relation of calcium to fat excretion in stools; children taking a mixed diet	201

INDEX TO VOLUME 19

	PAGE
Fales, H. L.: Calcium metabolism of infants and young children, and relation of calcium to fat excretion in stools; infants taking a modification of cow's milk.....	97
Fat, relation of calcium to fat excretion in stools; L. E. Holt, A. M. Courtney and H. L. Fales.....	97, 201
Feces, relation of calcium to fat excretion in stools; L. E. Holt, A. M. Courtney and H. L. Fales.....	97, 201
Feeding, Von Pirquet's feeding system; H. K. Faber.....	478
Fordyce's disease as pseudokoplik spots and cause of mistakes in diagnosis of measles; J. C. Regan.....	455
Foreign bodies in air and food passages; E. E. Graham.....	119
Fractures, treatment of birth fractures at Fordham hospital; S. W. Boorstein.....	375
Friedstein, H.: Water retention in pneumonia.....	337
Gastro-intestinal tract, roentgen-ray demonstration of abnormalities of, in children; C. G. Kerley.....	277
Goldbloom, A.: Improved needle for sinus therapy.....	229
Goldbloom, A.: Prognosis in operated cases of hypertrophic stenosis of pylorus	263
Graham, E. E.: Foreign bodies in air and food passages.....	119
Heart, auriculoventricular heart block in children, with report of case; J. A. E. Eyster and W. S. Middleton.....	131
Hemorrhage into spinal cord at birth; C. W. Burr.....	473
Hess, A. F.: Scorbutic beading of ribs.....	331
Holmes, J. B.: Recent work in anatomy, physiology and pathology of infancy and childhood.....	148
Holt, L. E.: Calcium metabolism of infants and young children and relation of calcium to fat excretion in stools; children taking a mixed diet.....	201
Holt, L. E.: Calcium metabolism of infants and young children, and relation of calcium to fat excretion in stools; infants taking a modification of cow's milk.....	97
Infant and child mortality, including miscarriages and stillbirths; H. Schwarz	249
Infant feeding, artificial infant feeding; give baby enough; M. Ostheimer.....	386
Infectious fevers, elimination of acetone bodies during; B. S. Veeder and M. R. Johnston.....	141
Injection, improved needle for sinus therapy; A. Goldbloom.....	229
Intestinal obstruction, case of anomaly of diaphragm, with herniation into thorax of certain viscera resulting in gastric and intestinal obstruction; L. R. DeBuys.....	55
Intestine, length of large and small intestine in young children; L. Robbin.....	370
Injections, fluid, in dehydrated infants; S. McLean and C. A. Lang.....	359
Johnston, M. R.: Elimination of acetone bodies during infectious fevers	141
Johnston, M. R.: Renal function in scarlet fever.....	223
Kerley, C. G.: Roentgen-ray demonstration of abnormalities of gastro-intestinal tract in children.....	277

INDEX TO VOLUME 19

	PAGE
Kidney function in scarlet fever; B. S. Veeder and M. R. Johnston.....	223
Kolmer, J. A.: Prenatal syphilis, with plea for its study and prevention..	344
Lang, C. A.: Fluid injections in dehydrated infants.....	359
Loughlin, R.: Antineuritic and growth stimulating properties of orange juice	349
Lungs, abscess of, in infants and children; H. Wessler and H. Schwarz..	137
Lusky, H. O.: Water retention in pneumonia.....	337
McClanahan, H. M.: Osteogenesis imperfecta congenita.....	181
MacLachlan, I. F.: Effect of intravenous injections of calcium in tetany and influence of cod liver oil and phosphorus in retention of calcium in blood	413
McLean, S.: Fluid injections in dehydrated infants.....	359
Mattill, P. M.: Dextrose tolerance in atrophic infants.....	42
Mayer, K. M.: Dextrose tolerance in atrophic infants.....	42
Measles, bullous eruption complicating measles; F. C. Neff.....	469
Measles, Fordyce's disease as pseudokoplik spots and cause of mistakes in diagnosis of measles; J. C. Regan.....	455
Meyers, A. E.: Dilatation of colon in children.....	167
Michael, M.: Résumé of literature on tuberculosis in children during 1918 and 1919.....	287
Middleton, W. S.: Auriculoventricular heart block in children, with report of case	131
Milk, food value of milk of water buffalo; W. W. Cadbury.....	38
Milk, hypersensitiveness to cow's milk; E. A. Park.....	46
Morse, J. L.: Report of two cases of congenital stricture of esophagus....	144
Mortality, infant and child mortality, including miscarriages and stillbirths; H. Schwarz.....	249
Needle, improved, for sinus therapy; A. Goldbloom.....	229
Neff, F. C.: Bullous eruption complicating measles.....	469
Nitrogenous and sugar content of blood of new-born; J. P. Sedgwick and M. R. Ziegler.....	429
Orange juice, antineuritic and growth stimulating properties of; A. H. Byfield, A. L. Daniels and R. Loughlin.....	349
Osteogenesis imperfecta congenita; H. H. McClanahan and W. W. Willard	181
Ostheimer, M.: Artificial infant feeding; give baby enough.....	386
Park, E. A.: Case of hypersensitiveness to cow's milk.....	46
Pathology, recent work in anatomy, physiology and pathology of infancy and childhood; J. B. Holmes.....	418
Phosphorus, effect of intravenous injections of calcium in tetany and influence of cod liver oil and phosphorus in retention of calcium in blood; A. Brown, I. F. MacLachlan and R. Simpson.....	413
Physiology, recent work in anatomy, physiology and pathology of infancy and childhood; J. B. Holmes.....	418
von Pirquet's feeding system; H. K. Faber.....	478

INDEX TO VOLUME 19

	PAGE
Pneumonia, water retention in; H. O. Lussy and H. Friedstein.....	337
Progress in pediatrics.....	62, 148, 230, 287, 392, 478
Protein, incidence of protein sensitization in normal child; H. M. Baker..	114
Pylorus, prognosis in operated cases of hypertrophic stenosis of pylorus; A. Goldbloom and R. C. Spence.....	263
Rachitis, craniotabes and beading of ribs as signs of; H. Schwarz.....	384
Regan, J. C.: Fordyce's disease as pseudokoplik spots and cause of mis- takes in diagnosis of measles.....	455
Respiratory diseases, review of literature on; L. C. Schroeder..	231
Respiratory tract, bacillus of Pfeiffer in inflammations of, in children; M. Wollstein and R. C. Spence.....	459
Ribs, craniotabes and beading of ribs as signs of rachitis; H. Schwarz	384
Ribs, scorbutic beading of ribs; A. F. Hess and L. J. Unger.....	331
Robbin, L.: Length of large and small intestine in young children... ..	370
Rodda, F. C.: Studies with a new method for determining coagulation time of blood in new-born.....	269
Sauer, L. W.: Dextrose tolerance in atrophic infants.....	42
Scarlet fever, renal function in; B. S. Veeder and M. R. Johnston.....	223
Schloss, O. M.: Allergy in infants and children.....	433
Schroeder, L. C.: Review of literature on respiratory diseases.....	231
Schwarz, H.: Abscess of lungs in infants and children.....	137
Schwarz, H.: Craniotabes and beading of ribs as signs of rachitis.....	384
Schwarz, H.: Infant and child mortality, including miscarriages and still- births	249
Scorbutus, beading of ribs in; A. F. Hess and L. J. Unger... ..	331
Sedgwick, J. P.: Nitrogenous and sugar content of blood of new-born..	429
Simpson, R.: Effect of intravenous injections of calcium in tetany and influence of cod liver oil and phosphorus on retention of calcium in blood	413
Sinus therapy, improved needle for; A. Goldbloom.....	229
Sodium cacodylate, results of some experimental work with, on athreptic infants; F. S. Clarke and A. Dow.....	260
Spence, R. C.: Bacillus of Pfeiffer in inflammations of respiratory tract in children	459
Spence, R. C.: Prognosis in operated cases of hypertrophic stenosis of pylorus	263
Spinal cord, hemorrhage into, at birth; C. W. Burr.....	473
Stillbirths, infant and child mortality; including miscarriages and still births; H. Schwarz.....	249
Sugar and nitrogenous content of blood of new-born; J. P. Sedgwick and M. R. Ziegler.....	429
Syphilis, prenatal, with plea for its study and prevention; J. A. Kolmer.	344
Tetany, effect of intravenous injections of calcium in, and influence of cod liver oil and phosphorus on retention of calcium in blood. A. Brown, I. F. MacLachlan and R. Simpson.....	413

INDEX TO VOLUME 19

	PAGE
Tuberculosis, résumé of literature on tuberculosis in children during 1918 and 1919; M. Michael.....	287
Unger, L. J.: Scorbutic beading of ribs.....	331
Urine, elimination of acetone bodies during infectious fevers; B. S. Veeder and M. R. Johnston.....	141
Veeder, B. S.: Elimination of acetone bodies during infectious fevers....	141
Veeder, B. S.: Renal function in scarlet fever.....	223
Wessler, H.: Abscess of lungs in infants and children.....	137
Wheeldon, T. F.: Study of achondroplasia, introducing new symptom—wedge-shaped vertebra	1
Willard, W. W.: Osteogenesis imperfecta congenita.....	181
Wollstein, M.: Bacillus of Pfeiffer in inflammations of respiratory tract in children	459
Ziegler, M. R.: Nitrogenous and sugar content of blood of new-born.....	429

The American Medical Association will pay thirty cents each for the following issues of the AMERICAN JOURNAL OF DISEASES OF CHILDREN: January, 1913; February, March, November and December, 1914; January and August, 1915; January, 1918; March and April, 1919. Address to AMERICAN MEDICAL ASSOCIATION, 535 North Dearborn Street, Chicago, Ill.

RJ American journal of diseases
1 of children
A5
v.19
cop.2

Biological
α Medical
Serials

PLEASE DO NOT REMOVE
CARDS OR SLIPS FROM THIS POCKET

UNIVERSITY OF TORONTO LIBRARY

STORAGE

